Relationship between terminal ileal pressure waves and propagating proximal colonic pressure waves

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Dinning, P. G., P. A. Bampton, M. L. Kennedy, and I. J. Cook. Relationship between terminal ileal pressure waves and propagating proximal colonic pressure waves. Am. J. Physiol. 277 (Gastrointest. Liver Physiol. 40): G983–G992, 1999.—The relationship between propagating distal ileal and proximal colonic motor patterns has not been systematically examined in humans. Our aim was to define the relationships, if any, between prolonged propagating contractions or discrete clustered contractions and cecal propagating sequences using multiple manometric recording sites spanning the distal ileum and unprepared colon. In 14 healthy volunteers, a 17-lumen-perfused silicon catheter was positioned perannally such that at least three recording sites lay in the ileum and the remainder in the colon. Intersidehole distance was 7.5 cm. In 271 h of recording, 30% of the terminal ileal propagating events was temporally associated with cecal propagating sequences. Significantly more prolonged propagating contractions (11 of 24, 46%; P = 0.02) were associated with cecal propagating sequences than were associated with ileal discrete clustered contractions (4 of 26, 15%). This trend was more pronounced at night. Of 159 cecal propagating sequences, 15 (9%) were preceded by an ileal propagating event. The remaining 91% was preceded by increased nonpropagating activity commencing 2 min before the cecal propagating sequence (P = 0.0002). We conclude that distal ileal propagating motor patterns are one stimulus for cecal propagating sequences, with the association being stronger for prolonged propagating contractions than for discrete clustered contractions.

ileum; colon; manometry; peristalsis; physiology

COLONIC PROPAGATING sequences (PS) are important in the stepwise movement of colonic content (2, 9, 17, 22), but the factors involved in the induction of this motor pattern have received little attention. Several observations suggest that a stimulus or stimuli to the cecum might be implicated in the genesis of at least some colonic PSs. For example, PSs are much more likely to originate in the cecum than at any other colonic site (9). Mucosal stimulation by chemicals, including bile acids (7) and laxatives (15, 23, 38), induces colonic PSs, which in some cases are Xylocaine sensitive (15). In addition, rapid changes in cecal pH and osmolality are likely to accompany bursts of ileal outflow, and changes in one or both have been shown to induce colonic propagating pressure waves (16).

Physical factors such as distension secondary to colonic filling are potentially implicated. For example, experimental proximal colonic lavage induces colonic motor activity in dogs (33), and colonic distension variably induces a peristaltic response (4). The arrival of a carbohydrate meal into the cecum induces local symptoms of irritable bowel syndrome (8), and similar symptoms have been reported in association with repetitive pressure waves in the ileum and cecum (25).

A number of previous studies have noted a temporal association between spontaneous distal ileal pressure patterns and cecal pressure waves (10, 25, 28, 31, 35). However, the possible temporal association of propagating motor patterns between the distal ileum and the proximal colon has not been systematically examined in the unstimulated human colon.

While making prolonged measurements of pressures throughout the unprepared human colon (11), we obtained prolonged recordings from multiple distal ileal and colonic sites, which permitted systematic examination of the possible relationships between propagating motor patterns in the distal ileum and those in the proximal colon. Our aims were to determine the extent to which migratory pressure patterns in the distal ileum are associated with colonic PSs, which originate in the cecum. Specifically, we hypothesized that propagating distal ileal motor patterns, either directly or indirectly, induce cecal PSs and that the association depends on the time of day or on the type of ileal motor pattern.

METHODS

Subjects. We studied a total of 14 healthy subjects (6 male and 8 female) with a mean age of 24.7 ± 5 yr who had no history of gastrointestinal complaints and who had normal bowel habits (defined as having between 2 bowel actions daily and 1 bowel action every 2 days). None had had previous abdominal surgery, other than appendectomy. None used regular medications, including laxatives. All gave written, informed consent, and the study was approved by the Human Ethics Committees of the South Eastern Area Health Service, Sydney, and the University of New South Wales.

Manometric technique. We used a 5-m-long, 17-lumen Silastic catheter with 16 recording side holes, each spaced 7.5 cm apart (Dentsleeve, Wayville, Australia). The overall catheter diameter was 3.5 mm, and each recording channel had an internal diameter of 0.5 mm. An additional core channel (0.8 mm ID) was used to infuse a latex balloon attached to the catheter tip. The catheter was rendered radiopaque by curing strips of barium paste to its exterior. Each recording lumen was perfused with degassed distilled water by a low-compliance pneumohydraulic perfusion pump at 0.15 ml/min (Dentsleeve). Before water perfusion was started, each channel was first flushed with CO2, which, due to its extreme solubility in water, ensured removal of any microbubbles within the catheter, thus minimizing compli-

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ance. Pressures were measured from each side hole with 16 external pressure transducers (Abbott Critical Care Systems, North Chicago, IL), and signals were amplified and digitized at 10 Hz by preamplifiers (AcqKnowledge III Software, BIOPAC Systems, Santa Barbara, CA) for later computer analysis (Apple Mac, LC 630, Cupertino, CA).

Study protocol. After an overnight fast, at 8:00 AM, the catheter tip was passed via the nose and through the pylorus under fluoroscopic control. The balloon was then inflated to a diameter of 2 cm, with a volume of air according to a previously determined volume diameter calibration curve. The catheter was advanced in increments of ~40 cm each hour or as needed. To prevent the catheter from looping in the stomach, the position and conformation of the catheter were checked fluoroscopically every 2 h. As the tip of the catheter approached the ileocolonic junction, the balloon was progressively deflated to a diameter of 0.5 cm to avoid impaction in the distal ileum. When the catheter tip had passed through the ileocolonic junction, the balloon was reinflated to a diameter of 2 cm. Recordings commenced at 2:00 PM on day 2 and continued for 24 h until 2:00 PM on day 3. At study completion, catheter position was again checked fluoroscopically before being removed, under sedation (2–5 mg midazolam), via the nose. Total fluoroscopy exposure time did not exceed 90 s, and the maximum whole body effective radiation dose equivalent was <1.6 mSv.

Subjects sat in bed during waking hours with the bed head elevated 45° and lay flat during sleep. They were asked to press an event key on a computer keyboard and note the time of onset in a diary at the onset of any sensations, including an urge to defecate, strain, onset of stool expulsion, an urge to pass flatus or the passage of flatus, or any other sensations that they perceived within the abdomen. They were also instructed to record times of ingestion of food or drink and the time of actual morning waking. Subjects were fed three standardized meals daily at 8:00 AM, 12:30 PM, and 5:30 PM as described previously, and these were consumed within 20 min (13).

Data analysis. The initial screening process involved 1) determination of regional baselines to which pressures within individual channels were referenced, 2) identification of artifact (i.e., strain) and strain patterns (see Other definitions), and 3) identification of candidate propagating pressure patterns in the ileum and colon, which were flagged and later subjected to closer scrutiny. The examination of the candidate propagating pressure patterns involved two steps: 1) examination of individual pressure changes within each channel in order to define individual “pressure waves” and “clusters” of pressure waves (defined below) and 2) consideration of the temporal relationships among similar pressure patterns in adjacent channels; if the criteria for propagation between adjacent channels were met, the pressure wave patterns were then qualified by the term “propagating.”

The baseline for each channel was established from segments of the trace when the subject was supine to identify the minimum, end-expiratory pressure for the 24-h recording period. All subsequent pressure measurements within each channel were referenced to each channel-specific baseline. Appropriate adjustments to the baseline were made at times when the subject altered body posture, such as assuming the supine posture at night, by adding or subtracting the pressure change induced acutely by the change in posture. For example, just before sleep, the subjects’ posture changed from a 45° head-up angle to the supine posture, resulting in a variable fall in baseline in each side hole, depending on the relative height of each side hole relative to the external pressure transducers. The acute fall in baseline at this moment was noted and was later added to all subsequent pressure values obtained while the subjects lay supine to correct for this systematic postural offset at night.

Each pressure change in each channel within a candidate propagating pressure pattern was first examined. A pressure wave was defined as a predominantly monophasic pressure change with a discernable onset, peak, and offset, which had an onset to peak amplitude of >5 mmHg and which did not have the features of pressure increases generated by artifact, straining, or respiratory oscillations (see Other definitions). The timing of pressure wave “onsets” (see Other definitions) was then determined. The temporal relationship among pressure waves in adjacent channels was then considered to determine whether the combination of pressure waves would meet the criteria for propagation based on the following velocity criteria for either the colon or the ileum. Pressure waves were deemed to be propagating if the conduction velocity between wave onsets within a sequence of waves in three or more adjacent recording sites lay between 0.2 and 12 cm/s. If these criteria for propagation were met in the colon, the array was termed a “colonic propagating sequence” (PS) and the individual pressure waves within a PS were then called colonic “propagating pressure waves.” Each PS was further qualified as antegrade or retrograde according to the direction of propagation. If an array of monophasic ileal pressure waves were registered at three or more adjacent recording sites and if the above criteria for propagation were met, then this sequence of ileal pressure waves was called an ileal “prolonged propagating contraction” in keeping with previous descriptions of this motor pattern (31).

Rhythmic ileal (i.e., multiphasic and repetitive) pressure patterns were considered to propagate if an array of three or more bursts of such pressure waves, each of at least 50-s duration and frequency of its component waves of 4–12 cpm, were recorded from adjacent recording sites and the conduc-

Other definitions. A “strain pattern” was defined as a change in pressure detected at multiple intraluminal recording sites that are consistent with extraluminal mechanical influences generated by the subject (e.g., cough, body movement, strain). A strain pattern was distinct from passive alterations in pressure secondary to alterations in body posture or posture (see Data analysis) and was defined as a pressure wave with rapid upstroke, which was identical in shape and which was registered simultaneously across all recording channels. Strain patterns occurring during an epoch in which the area under the pressure curve was to be calculated were removed from the trace, and a value equivalent to the average for the remainder of that epoch was then assigned in place of the removed segment. The term “artifact” was used to describe recorded signals from extracorporeal mechanical or electrical events that were not detected by a side hole (e.g., catheter movement, equipment adjustments). Respiratory oscillations were defined as sinusoidal pressure oscillations, identical in at least four channels with a frequency of 8–12 cpm, or those that were consistent with the respiratory rate of the subject at the time of the study.

Measurements. We designated up to five terminal ileal recording sites, with the site closest to the ileocolonic junction always designated ileal region 5 and the most proximal site designated ileal region 1. Distinction between ileal and colonic pressure tracings was readily apparent from the morphology of the respective regional patterns. This distinction was facilitated by compressing the tracing to appreciate
the characteristic small bowel motility pattern. If the catheter migrated proximally or distally during the study, the relative movement of the most distal side hole within the ileum was readily apparent from changes in the appearance of the tracings.

The 24-h recording period was divided into three component recording periods: 1) nocturnal (11:00 PM on day 2, time of first waking day 3), 2) postwaking (the 2-h interval from time of first waking the morning of day 3), and 3) daytime (the remainder of the recording hours). These temporal subdivisions were made to permit closer examination of potential ileocolonic relationships at times of the day when the prevalence of ileal and colonic pressure patterns is known to vary.

We quantified the following for each of the four motor patterns, which were defined in Data analysis: the site of origin, the distance propagated, velocity of propagation, and the amplitude of each pressure wave recorded at each region. These measures were also coded for each of the three time periods in each subject before calculating time- and region-specific group mean values for statistical analysis. Every terminal ileal propagating event that propagated up or beyond region T4 (i.e., within 2 side holes of the ileocolonic junction) was considered for analysis. Within each ileal discrete clustered contraction, we also determined the number and frequency of individual pressure waves.

The potential temporal association between ileal and cecal propagating events was assessed by measuring the time lag between the most distal ileal pressure wave onset and that of the subsequent cecal event. The two events were considered to be temporally associated if the onset of the cecal pressure wave occurred within 60 s after the onset of the ileal pressure wave at the most distal ileal recording site. We hypothesized that if a cecal PS was not temporally associated with an ileal propagating pressure event then it might be preceded by a general increase in distal ileal motor activity. To examine this possibility, we calculated the area under curve (AUC) within each distal ileal side hole for each 1-min epoch for 10 min beyond region T4 (i.e., within 2 side holes of the ileocolonic junction) was considered for analysis. Within each ileal discrete clustered contraction, we also determined the number and frequency of individual pressure waves.

Statistical analysis. A $\chi^2$ statistic was used to make inferences about differences between proportions of wave types between ileum and colon and about proportions of temporally associated patterns among the three time periods and among pattern type. Statistical inferences about possible changes in ileal AUC values preceding the onset of a cecal PS were made by comparing the AUC value for each 1-min epoch, commencing with that immediately before the onset of the cecal PS, with baseline ileal AUC using a Student’s paired t-test and the Bonferroni correction factor for multiple comparisons.

Baseline ileal AUC was the value averaged over a 5-min interval commencing 10 min before the onset of the cecal PS, which had first shown no differences among each of the five 1-min epochs within this baseline interval using a repeated-measures ANOVA. All data are expressed as means ± SE unless stated otherwise.

RESULTS

In the 14 subjects at the commencement of recording (2:00 PM, day 2), the catheter tip lay at or distal to region 8 (splenic flexure) in all, within the descending colon in five, within the sigmoid colon in three, and within rectum in two subjects. Data from all 14 subjects were analyzed. However, in two subjects, all the proximal side holes migrated into the colon during the evening of day 2, precluding inclusion of the data from the postwaking and daytime periods in these two subjects. Hence, a total 271.3 h of recording time (19.3 ± 1.3 h/subject) was analyzable, comprising 95.9 h during the nocturnal period (7.3 ± 0.4 h/subject; range 4.1–9 h), 151.5 h during the daytime period (10.8 ± 0.8 h/subject; range 4.8–14.5 h), and 22 h during the postwaking period (2.0 ± 0.0 h/subject). Thirteen of 14 subjects defecated during the recording period.

Colonic PSs. In the 14 subjects, we detected a total of 553 colonic PSs, 159 (29%) of which originated in the cecum (Table 1). The highest frequency of cecal PSs was observed in the postwaking period, during which average frequency was double that seen during the daytime period. The frequency of cecal PSs was not influenced by meals and did not increase before or after defecation.

Terminal ileal propagating pressure waves. There was a total of 50 terminal ileal propagating events in the 14 subjects: 24 prolonged propagating contractions (Fig. 1) and 26 discrete clustered contractions (Fig. 2, Table 1). The average frequency of all propagating ileal

| Table 1. Frequency of propagating terminal ileal events and cecal propagating sequences |
|--------------------------------|----------------|----------------|----------------|----------------|
| Pressure Wave Type | Prolonged Propagating Contraction | Discrete Clustersed Contractions | Total Ileal Events | Total Cecal PSs |
| Postwaking period | | | | |
| Period total | 2 | 8 | 10 | 23 |
| Number·subject | $0.07 \pm 0.07$ | $0.25 \pm 0.12$ | $0.3 \pm 0.1$ | $1.0 \pm 0.4$ |
| Daytime period | | | | |
| Period total | 8 | 5 | 13 | 94 |
| Number·subject | $0.07 \pm 0.03$ | $0.03 \pm 0.1$ | $0.1 \pm 0.03$ | $0.5 \pm 0.06$ |
| Nocturnal period | | | | |
| Period total | 14 | 13 | 27 | 42 |
| Number·subject | $0.08 \pm 0.08$ | $0.13 \pm 0.05$ | $0.3 \pm 0.1$ | $0.4 \pm 0.08$ |
| Study total/average | | | | |
| Study total | 24 | 26 | 50 | 159 |
| Number·subject | $0.1 \pm 0.06$ | $0.1 \pm 0.02$ | $0.2 \pm 0.05$ | $0.6 \pm 0.04$ |

Values are means ± SE. Postwaking period is the 2-h immediately following the time of first morning waking by each subject. Daytime period is period from end of postwaking interval up to 11:00 PM. Nocturnal period is period from 11:00 PM to first morning waking by individual subjects. Period total is total number of each pressure wave type in all 14 subjects. Group mean wave frequencies were averaged over the period specified. PS, propagating sequence.
events (0.2 ± 0.05 events·subject⁻¹·h⁻¹) was roughly one-third that of cecal PSs (0.6 ± 0.04 events·subject⁻¹·h⁻¹).

In contrast to the nocturnal suppression of cecal PSs, the average nocturnal frequency of ileal propagating events (0.3 ± 0.1 events·subject⁻¹·h⁻¹) was three times that seen during the daytime (0.1 ± 0.03 events·subject⁻¹·h⁻¹). The frequency of ileal propagating events was not influenced by either defecation or meals.

Temporal relationship between ileal and cecal pressure waves. Overall, 30% of terminal ileal propagating events was temporally associated with cecal PSs (Table 2). A significantly greater proportion of prolonged propagating contractions (11 of 24, 46%; P = 0.02) was temporally associated with cecal PSs than discrete clustered contractions (4 of 26, 15%) (Table 2, Fig. 3). None of the 11 discrete clustered contractions at night was associated with cecal PSs, suggesting a tendency toward a nocturnal dissociation between these two motor patterns when compared with the daytime (2 of 5) or postwaking periods (2 of 8) (P = 0.07). Furthermore, during the nocturnal period, significantly more prolonged propagating contractions (7 of 14) were associated with cecal PSs compared with discrete clustered contractions (0 of 13; P = 0.003) (Table 2).

Of 159 cecal PSs, 15 (9%) were temporally associated with a preceding ileal propagating event (Table 2). There was a tendency for a greater proportion of nocturnal cecal PSs (7 of 42, 17%) to be temporally associated with ileal events than daytime PSs (5 of 94, 5%) or post-waking PSs (3 of 23, 13%), but these differences did not reach statistical significance (P = 0.09).

Because we had no gastric or proximal small bowel recording sites, we were not able to identify with certainty any terminal ileal migrating motor complex (MMC) phase III activity. However, 4 of 26 discrete clustered contractions demonstrated rhythmic activity...
that persisted uninterrupted for at least 3 min, which were recorded in all ileal side holes; none of these was temporally associated with cecal PSs. The duration and appearance (Fig. 4) of these events would be consistent with previously defined phase III activity (24, 26). For example, the mean duration of these four rhythmic events (12.5 ± 1.6 min, range 5.5–39.9 min) was significantly longer than that of the remaining 22 discrete clustered contractions (2.6 ± 1.1 min, range 0.9–6.1 min) (P = 0.003). The propagation velocity of these four prolonged rhythmic events (0.02 ± 0.005 cm/s) was significantly slower (P = 0.0001) than that of the remaining 22 discrete clustered contractions (0.23 ± 0.04 cm/s).

AUC. There were 144 cecal PSs that were not temporally associated with an ileal propagating event. We examined area under the pressure curve at each distal ileal site in the 10-min period leading up to and following the onset and completion of each of these cecal PSs, which were not temporally associated with an ileal propagating event. That is, this analysis did not include the 15 of 159 cecal PSs for which a temporally associated ileal propagating event was identified. There was a steady increase in the AUC commencing 4 min before the onset of these cecal PSs (Fig. 5). This phenomenon was dependent on proximity to the ileocolonic junction and was only apparent at the two most distal ileal sites, that is, within 10.5 cm of the ileocolonic junction. This effect was statistically significant (P = 0.0002) in the two 1-min epochs preceding the cecal PS at the ileal site 3 cm from the ileocolonic junction and for 1 min preceding the cecal PS at the site 10.5 cm proximal to the ileocolonic junction (P = 0.038). This pattern was evident in all three time periods, although the effect was less marked at night.

DISCUSSION

This study, to our knowledge, is the first to systematically examine the temporal relationships between ileal propagating and nonpropagating motor patterns and cecal propagating pressure wave sequences in the unprepared human colon over a 24-h period. The major findings of this study were that the terminal ileal activity displays an overall increase immediately before the initiation of cecal PSs and that 30% of terminal ps...
ileal propagating events is temporally associated with cecal PSs. The ileal prolonged propagating contraction has a higher rate of temporal association (46%) with cecal PSs compared with the ileal discrete clustered contractions (15%). Discrete clustered contractions showed a tendency to nocturnal "dissociation" from cecal PSs, whereas the only ileal pattern to be associated with cecal PSs during the nocturnal period was the prolonged propagating contraction. These data suggest that propagating ileal motor patterns are one stimulus for cecal PSs.

Several previous human manometric studies used recordings that focused on the distal ileum and ileocolonic junction and, in some cases, had one or more side holes that recorded proximal colonic pressures (10, 25, 28, 31, 35). However, none of these studies was designed to examine the direct relationship between ileal activity and colonic propagating motor patterns. Indeed, the majority either utilized only one proximal colonic recording site or employed insufficient colonic recording sites with a constant intersidehole spacing to reliably register propagating colonic pressure waves (10, 25, 28, 31). One study that used two or three proximal colonic recording side holes spaced at 4-cm intervals did not report any propagating colonic pressure waves nor any temporal relationship between ileal and colonic pressure waves (35). Nonetheless, some of these studies did note that distal ileal pressure waves were sometimes associated with cecal pressure waves (10, 25, 31) and that this phenomenon was also noted in response to stimulation by ileal short-chain fatty acid infusion (21) or distal ileal distension (12). MMCs, which are very uncommon in the human terminal ileum, have only rarely been reported to cross into the cecum (31). Without the benefit of gastric or proximal small bowel recording sites in the present study, we could not identify with certainty any terminal ileal MMC phase III activity. However, we did identify four rhythmic events that were markedly prolonged and had a slow conduction velocity; this raises the possibility that these four events might have been phase III activity. None of these four events was temporally related to colonic PSs (Fig. 4).

The temporal association between ileal and colonic propagating events seems to be stronger in the canine than in the human colon. For example, Quigley et al. (31) showed that 50% of ileal discrete clustered contractions and 76% of ileal prolonged propagating contractions continued propagating in the proximal canine colon.

It is highly unlikely that the observed 30% association between ileal and cecal propagating events in the present study can be accounted for by chance. Both ileal propagating events and cecal PSs are infrequent, occurring with frequencies of only 0.2 ± 0.05 and 0.6 ± 0.04 events·subject⁻¹·h⁻¹, respectively. These frequencies, combined with the narrow time window (60 s) adopted as necessary for temporal association between these events, mean that the probability that 30% of the events occurred together purely by chance is extremely remote.

PSs can originate at any site along the colon, but the majority arise in the cecosigmoid colon (9). This observation suggests that either local stimuli unique to the cecum might initiate PSs in this region or that the cecum displays a higher intrinsic sensitivity to such stimuli than do more distal colonic regions. The full repertoire of stimuli capable of initiating colonic PSs remains unclear. Extrinsic neurogenic or humoral influences are likely to contribute. For example, PS frequency is dramatically reduced during stable sleep and is promptly stimulated by nocturnal arousal and early morning waking, suggesting that input from the central nervous system is one such important stimulus.

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**Table 2. Frequency of association between cecal PSs and ileal propagating events**

<table>
<thead>
<tr>
<th>Pressure Wave Type</th>
<th>Prolonged Propagating Contractions</th>
<th>Discrete Clustered Contractions</th>
<th>Total Ileal Events</th>
<th>Total Cecal PSs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postwaking period</td>
<td>2 (1)</td>
<td>8 (2)</td>
<td>10 (3)</td>
<td>23 (3)</td>
</tr>
<tr>
<td>Period total</td>
<td>30%</td>
<td>13%</td>
<td>38%</td>
<td>15%</td>
</tr>
<tr>
<td>Nocturnal period</td>
<td>14 (7)</td>
<td>5 (2)</td>
<td>27 (7)</td>
<td>42 (7)</td>
</tr>
<tr>
<td>Period total</td>
<td>26%</td>
<td>17%</td>
<td>30%</td>
<td>9%</td>
</tr>
</tbody>
</table>

Period and study total give total number of each pressure wave type in all 14 subjects. Numbers in parentheses indicate number of ileal events associated with cecal PS. Numbers in brackets indicate number of cecal PS associated with ileal events. Numbers in brackets indicate number of ileal events associated with cecal PSs.
Furthermore, evidence exists, albeit conflicting, of a cephalic phase of the gastrocolonic response (32, 37). There is also some evidence for a centrally mediated sympathetic brake on colonic phasic activity (14).

Local intraluminal (mechanical and chemical) mechanisms are also involved in the initiation of propagating colonic motor patterns. Contractile responses of colonic smooth muscle in vitro are extremely sensitive to stretch (19), and colonic balloon distension in vivo has a variable and somewhat region-dependent capability for the induction of colonic propagating pressure waves (3, 4). Dihydroxy bile acids and laxatives acting via mucosal receptors induce propagating colonic activity (1, 15, 18, 20, 23, 30, 38). Hence, propulsion of ileal chyme into the cecum by propagating ileal pressure waves might be one factor capable of inducing colonic PSs, either by the mechanism of cecal distension or via mucosal afferent stimulation.

There are two plausible mechanisms to account for the observed association between ileal and cecal propagating events. Cecal filling as a consequence of ileal propagating activity may secondarily initiate cecal PSs. Alternatively, the phenomenon may represent a direct neurogenically mediated extension of the peristaltic reflex across the ileocolonic junction. It is unlikely that an independent factor(s) is acting periodically and simultaneously on both adjacent regions to induce similar motor patterns because the observed response would be expected to be simultaneous and not sequential as is observed.

It is possible that intermittent bursts of ileocolonic flow, in response to ileal propagating pressure waves or other less recognizable motor patterns, might initiate cecal PSs. At least in the dog, discrete clustered contractions and prolonged propagated contractions have been shown to be effective mediators of ileal emptying (29). Scintigraphic studies have demonstrated that ileocolonic flow is intermittent and occurs most frequently around 90 min after a meal (5, 28, 34–36), but fasting ileocolonic transit in humans tends to be erratic (35) and, unlike in the dog, has no association with interdigestive MMCs (36). Hence, it remains uncertain whether terminal ileal propagating pressure waves or clusters mediate bursts of ileocolonic flow in humans. We previously noted a close temporal relationship between distal prolonged propagating contractions and bursts of flow from temporary ileostomies fashioned ~10 cm proximal to the human ileocolonic junction, suggesting that these events occur in humans (12). On the other hand, Spiller et al (35), who measured cecal filling scintigraphically, could not relate ileal motor patterns to episodes of cecal filling. The findings of the present study further militate against this concept. The majority of ileal propagating events in the present study occurred during fasting (nocturnal or postwaking) periods, and there was no postprandial increase in cecal PS frequency nor in the association between ileal events and cecal PSs. Nonetheless, even in the absence of ileal propagating pressure waves, we did demonstrate a general increase in distal ileal pressure immediately before the onset of cecal PSs. It remains entirely possible that nonpropagating or less recognizable ileal pressure patterns might promote episodic ileocecal flow and thereby stimulate cecal PSs.

Ileal instillation of short-chain fatty acids induces migratory pressure waves that propagate smoothly...
across the ileocolonic junction and extend as far as the splenic flexure (21). This suggests that the intramural neuromuscular control mechanism does exist that mediates the direct transmission of a terminal ileal peristaltic reflex through to the colon. An analogous “seamless” transition of propagating pressure waves has also been observed across the pylorus into the duodenum (6), strongly supporting the hypothesis that neural pathways span these sphincters.

The frequency of colonic PSs drops dramatically at night, particularly during stable sleep (13). In contrast, the present study shows no such nocturnal suppression of distal ileal propagating events. As a consequence, the relative importance of ileal events in the genesis of cecal PSs tends to be greater at night than it is during the daytime. The proportion of cecal PSs that are preceded by ileal propagating events increased from a daytime value of 5% to 17% at night. These combined observations also suggest that the colon might need to be rendered “receptive” by a certain level of central nervous system input before additional factors, including those associated with terminal ileal motor patterns, are able to trigger a colonic PS. Notwithstanding, the colon at night seems relatively unresponsive to discrete clustered contractions, as this particular pattern never preceded a nocturnal colonic PS, although it retained its nocturnal responsiveness to prolonged propagating contractions (Table 2).

In the present study, 70% of all ileal propagating events was not associated with cecal PSs. It is possible that we could not detect all cecal PSs using our manometric method, perhaps because of the size and geometry of the cecum. However, von der Ohe et al. (39) showed that a manometric catheter was as sensitive as a barostat in detecting phasic events within lumina <5.6 cm in diameter. We had no way of measuring cecal diameter in the present study, but it was unlikely to have been >5.6 cm, since we recorded separate ileal events that were both associated and unassociated with cecal PSs in the same patient. We were confident of

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**Fig. 5.** Area under the curve (AUC) measurements at 3 distal ileal sites before and after onset and completion of propagating sequences originating in the cecum, represented by horizontal bars. Numbers in parentheses (in cm) indicate distance of the ileal side hole from the ICJ. Note that there is a region-dependent increase in ileal AUC leading up to onset of the cecal propagating sequence. This effect was statistically significant (after Bonferroni correction factor was applied) at the distal sites for 2 min before and in the adjacent ileal site for 1 min before onset of the cecal propagating sequence.
catheter placement with regard to side holes in the ileum and colon, as has been shown in Fig. 1. Although ileal events are likely to be one factor contributing to the genesis of cecal PSs, it is clearly not the only one. Only 9% of all cecal PSs was confirmed to be associated with ileal propagating events. However, it is likely that there is some form of association between the terminal ileum and the cecal PS because we recorded a significant increase in the terminal ileal nonpropagating activity. Therefore, at least within the limitations of the present study, more than 90% of cecal PSs are likely to be attributable to other as yet unrecognized factors.

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