

Normal aspects of colorectal motility and abnormalities in slow transit constipation

Gabrio Bassotti, Giuseppe de Roberto, Danilo Castellani, Luca Sediari, Antonio Morelli

Gabrio Bassotti, Giuseppe de Roberto, Danilo Castellani, Luca Sediari, Antonio Morelli, Gastroenterology and Hepatology Section, Department of Clinical and Experimental Medicine, University of Perugia Medical School, Perugia, Italy
Correspondence to: Dr. Gabrio Bassotti, Strada del Cimitero, 2/a, 06131 San Marco Perugia, Italy. gabassot@tin.it
Fax: +39-75-5847570
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Abstract

Human colonic motility is a relatively difficult topic to investigate. However, the refinement of manometric techniques in recent years enabled us to study both the proximal and distal segments of the viscus. The present paper reviews our knowledge about normal aspects of colorectal motility in man and the abnormalities found in slow transit constipation (STC), one of the most frequent and difficult to treat subtypes of constipation. An internet-based search strategy of the Medline and Science Citation Index was performed using the keywords colon, colonic, colorectal, constipation, slow transit, motility, rectal, rectum in various combinations with the Boolean operators AND, OR and NOT. Only articles related to human studies were used, and manual cross-referencing was also performed. Most of colonic motor activity is represented by single nonpropagated contractions, rarely organized in bursts; this activity is maximal during the day, especially after waking and following meals. In addition, a specialized propagated activity with propulsive features is detectable, represented by high- and low-amplitude propagated contractions. In the severe form of constipation represented by the slow transit type, the above motor activity is completely deranged. In fact, both basal segmental activity (especially in response to meals) and propagated activity (especially that of high amplitude) are usually decreased, and this may represent a physiologic marker of this disorder. Human colonic motor activity is quite a complex issue, still only partly understood and investigated, due to anatomic and physiological difficulties. In recent years, however, some more data have been obtained, even in proximal segments. These data have helped in elucidating, although only in part, some pathophysiological mechanisms of chronic constipation, and especially of the STC subtype.

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INTRODUCTION

The main physiological properties of the human colon (absorption, propulsion of contents, storage and expulsion of feces) require unique motor activities, different from those of the upper gut^[1], apt to propel distally intraluminal contents, to mix them in a continuous manner, and to store and eventually expel the residuals^[2]. Since colonic contents, unlike those in the upper gut, employ hours or days to pass through the viscus, prolonged observations (24 h or more) are needed to assess the various aspects of colonic motility^[3].

Several techniques have been proposed to evaluate the motor behavior of the large bowel for prolonged periods of time^[4-6], the more diffuse being colonic manometry as both a research and (especially in the pediatric area) diagnostic tool^[7,8]. The more frequently employed technique consists of positioning a manometric catheter within the colon by the aid of a colonoscope; the catheter is then connected to a recording apparatus to detect intraluminal pressures throughout the day, and to evaluate the effects of meals, sleep, awakening, etc.^[9]. More recently, the classic water-perfused catheters were compared to solid state ones^[10] that allow prolonged ambulatory recordings of colonic motility^[11,12] and even an automated computer analysis of recordings^[13].

SEARCH STRATEGY

An internet-based search strategy of the Medline and Science Citation Index was performed using the keywords colon, colonic, colorectal, constipation, slow transit, motility, rectal, rectum in various combinations with the Boolean operators AND, OR and NOT. Only articles related to human studies were used, and manual cross-referencing was also performed. Articles published in English between January 1965 and March 2004 were selected; however, a search in non-English languages and in journals published before 1965 was also performed in our library. Letters and abstracts were quoted only when the full papers were not available.

BASIC ASPECTS OF NORMAL COLONIC MOTILITY IN HUMANS

Manometric investigations have shown that colonic motility may be grossly classified into two main types, and that these mostly agree with previous radiological observations^[14]. We

have recently proposed a simple classification of colonic contractile patterns, based on our experience with 24-h recordings in healthy humans^[9,15]. Colonic motility may therefore be divided into *segmental activity* (single contractions; bursts of contractions: rhythmic, arrhythmic) and *propagated activity* (low-amplitude propagated contractions (LAPC); high-amplitude propagated contractions (HAPC)).

Segmental activity

This kind of contractile activity constitutes mostly of the overall colonic motility, and it is usually represented by waves with amplitude ranging from 5 to 50 mmHg; occasionally, contractions of higher amplitude may be observed (Figure 1). Segmental contractions may appear singly or grouped (bursts); although the bursts appear usually as an arrhythmic array of waves, in a small percentage of time (<6% of the overall contractile daily activity) they may assume a rhythmic frequency. This rhythmic frequency is mostly comprised in the 3 cycle/min range, and it is preferentially observed in the distal (descending and sigmoid colon)^[16]. The purpose of the segmental contractile activity is to propel distally the fecal matter by means of an aborally directed pressure gradient that moves slowly the contents toward the rectum^[17,18]. This activity also allows an optimal absorption of water, electrolytes, short-chain fatty acids, and bacterial metabolites.

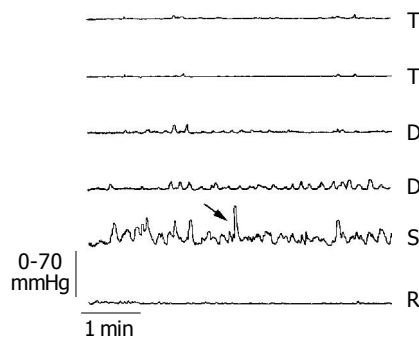


Figure 1 Representative manometric tracing of normal colonic segmental activity. Note that most contractions feature low amplitude, with sporadic ones (arrow) exceeding 50 mmHg. Recording points are 12 cm apart, and span from the transverse colon (T) to the rectum (R).

Propagated activity

To date, objective criteria (also employing automated analysis) to distinguish the various types of propagated contractions do not exist^[19]. We have classified the propagated events, on the basis of their amplitude, as LAPC and HAPC. The former (Figure 2) that feature an amplitude of less than 50 mmHg and are relatively frequent (on average, more than 100 events/d) have a probable main function of transporting fluid contents within the colon^[20,21]; LAPC have also been associated with distension of the viscus^[22] and passage of flatus^[23]. The other kind of propagated activity, represented by contractions averaging more than 100 mmHg amplitude (Figure 3) and occurring infrequently (on average, about 6 events/d), was firstly described in man by radiologists at the beginning of the last century^[24], and was subsequently demonstrated to correspond to the radiological concept of

“mass movements”, able to shift large quantities of contents for a long tract within the colon^[25,26]. More recently, HAPC have been better characterized by manometric means^[27,28], and their important role in the defecatory mechanisms established. These powerful contractions, in fact, are strongly associated with the defecation itself, and precede the expulsion of stools, so that they are considered one of the driving events of this important physiologic act^[29,30].

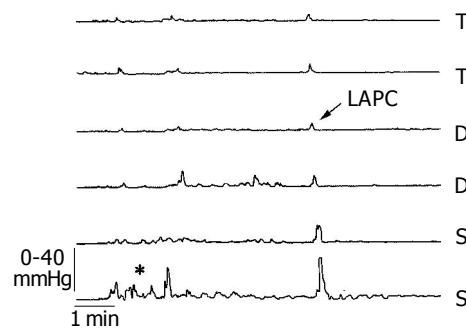


Figure 2 Representative manometric tracing showing a LAPC (arrow). Note also, in the last tracing, the presence of a burst of segmental sigmoid activity (asterisk). Recording points are 12 cm apart, and span from the transverse (T) to the sigmoid colon (S).

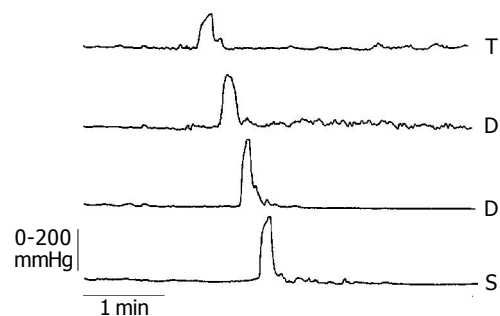


Figure 3 Representative manometric tracing of a HAPC. Note that the amplitude of the propagated sequence is well distinct with respect to the background segmental activity. Recording points are 12 cm apart, and span from the distal transverse (T) to the proximal sigmoid colon (S).

Daily organization of colonic motility and relationships with physiologic events

Unlike the upper gut, the human colon seems not to be organized in accordance to regular motor patterns that follow a cyclic timing. However, in recent years periodic motor phenomena have been documented in the rectum (“rectal motor complex”, RMC)^[31] and in the more distal colonic segments (“periodic colonic motor activity”) (Figure 4)^[32]. The physiological significance of these phenomena is still under investigation, although for the RMC a continence-preserving mechanism (especially when sleeping) has been hypothesized^[33]. No cyclic or periodic motor activity has been documented in the anal canal^[34].

More information is available concerning the fluctuations of colonic motor activity around-the-clock: in fact, prolonged manometric and electromyographic recordings have convincingly

shown that a circadian trend is recognizable, with a maximum of activity during the daylight hours, after awakening in the morning, and after meals^[4,5]. Conversely, sleep causes a profound inhibition of colonic motility, and seems to represent a major determinant of its diurnal variations^[35,36]. These variations in colonic motility are paralleled by a similar trend that may be observed in the tonic activity of the viscus' wall when measured by means of a barostat^[37].

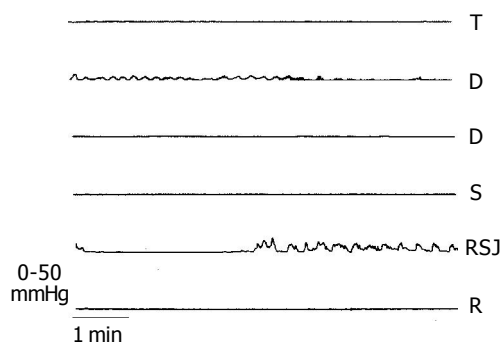


Figure 4 Representative manometric tracing showing two episodes of periodic colonic motor activity (asterisks) occurring independently at different colonic levels (proximal descending colon and rectosigmoid junction, respectively). Recording points are 12 cm apart, and span from the transverse colon (T) to the rectum (R).

The ingestion of food is a major physiological stimulus for colonic motor activity^[38], and it is represented by an increase (of at least 2-h duration) in the overall motility following the first mouthful of food (Figure 5)^[39]; this response, mostly represented by segmental contractions, is also accompanied by an increased smooth muscle tone^[40]. The colonic motor response to eating is driven by a dual component, cerebral and gastric, in that it may be evoked by both sham feeding and gastric distension^[41]. Meal composition influences colonic motor response: in fact, although carbohydrate meals are able to elicit motor activity, the effects are short lived when compared with fat meals^[42].

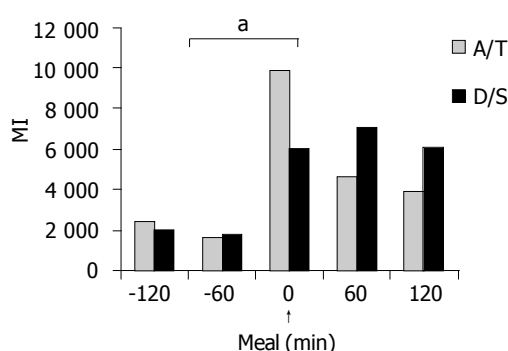


Figure 5 Colonic motor response to eating in normal subjects. All post-meal values (asterisk) are significantly ($P < 0.05$) different with respect to basal values in both proximal (A/T) and distal (D/S) segments. MI, motility index.

SLOW TRANSIT CONSTIPATION: DEFINITION

Constipation is a frequent clinical symptom, and its

diagnostic criteria have been recently revised in the Rome II classification^[43] as the presence in the last year, for at least 12 wk (which need not be consecutive) and in more than 1/4 of defecations, of two or more of the following: straining, lumpy or hard stools, sensation of incomplete evacuation, sensation of anorectal obstruction/blockade, manual maneuvers (digital evacuation, support of the pelvic floor, *etc.*) to facilitate defecation, and/or less than three defecations per week. Loose stool are not present and there are insufficient criteria for irritable bowel syndrome.

Two major pathophysiologic subtypes of constipation may be identified, with a third being the coexistence of both in the same patient^[44]. The most frequent subtype is represented by the pelvic floor dysfunction (also known as "outlet obstruction", "obstructed defecation", "dyschezia", "anismus", "pelvic floor dyssynergia"), which features normal or slightly slowed colonic transit with residual storage in the rectum or rectosigmoid area^[45]. The main pathophysiologic mechanism is due to an inability to evacuate adequately contents from the rectum, and it will not be discussed further, since it has been recently reviewed extensively elsewhere^[46]. The other subtype of constipation is the so-called slow transit constipation (STC), a clinical syndrome usually affecting women and characterized by often intractable constipation and heavily delayed colonic transit^[47]; this condition is usually attributed to disordered colonic motor function^[48]. In the last years, STC had been the subject of several investigations, aimed at evaluating the motility abnormalities of the large bowel as responsible for the patients' complaints. These pathophysiological aspects of STC will be discussed below. We feel that many of the available data are quite significant because (and differently than those available for other subtypes of constipation or other functional diseases of the large bowel) they have often been obtained in relatively homogenous cohorts of patients.

COLONIC MOTOR ABNORMALITIES IN STC

Although the etiology of STC remains elusive, there is ample evidence that motility of the large bowel is profoundly deranged in this condition, and this derangement may be observed for almost all the physiologic variables described above.

Segmental activity

Most of the few studies available were limited to the anorectal-sigmoid area (thereby justifying in part the heterogeneity of findings). These studies showed either overall reduced rectosigmoid motility^[49] and impaired response to intrarectal bisacodyl^[50], or normal or increased rectosigmoid motor activity^[51]. More recently, investigations on more proximal segments of the colon have demonstrated that in these patients the segmental contractile response to cholinergic stimulation is heavily impaired^[52] and that the regular contractile frequency activity is reduced to about half (i.e., <3%) of that recorded in normal subjects^[53].

Propagated activity

Data on LAPC in STC are still scarce; we have recently shown that this activity may be preserved in such patients,

thereby acting as a sort of alternative mechanism able to vicariate, at least in part, the severely impaired main propulsive force (see below)^[54]. Conversely, there are several observations showing that HAPC activity is usually deranged, up to complete absence of such events, in severely constipated patients, and especially in those with STC^[55-59]; this impairment consists of both a decreased average daily number of HAPC (Figure 6) and decreased amplitude and duration. The latter finding is consistent with the report that HAPC amplitude is a major factor for the propulsion of colonic contents to the rectum^[18]. In extreme cases, such an activity is completely absent, and it is also accompanied by almost complete disappearance of the segmental contractile activity: these are the patients with true “colonic inertia”, in whom no medical therapy is successful, and surgical intervention is often the only choice^[60,61].

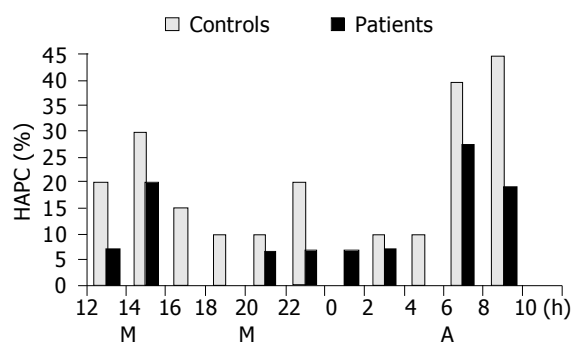


Figure 6 Percentage and distribution of HAPC/24 h in control subjects and severely constipated patients. M, meal, A, awakening. Adapted from Ref.^[65].

Daily organization of colonic motility and relationships with physiologic events

Concerning RMC and periodic colonic motor activity, there is evidence that this kind of activity may be abnormal in STC, with a decreased periodicity and reduced frequency^[59,62,63]. A recent investigation, however, reported that these patients may display excessive and un-coordinated RMC activity that, added to the reduced propulsive activity discussed above, may further delay the flow of colonic contents into the rectum^[64]. Looking at the daily motor activity, a study showed an overall decrease of colonic contractile activity^[65], although the day-night cycle seemed to be maintained, suggesting that normal circadian trend may be preserved, as also shown by a normal contractile response following sudden awakening from sleep^[66].

Some of the main physiological reflexes appear to be deranged in STC. In fact, an abnormal motor response to eating seems to be a constant feature in these patients, as shown by both electromyographic and manometric studies consistently demonstrating an overall scarce response to meal ingestion^[67-69]. This response is also characterized by a significant impairment of both segmental and propagated activity that follows the meals with respect to that observed in healthy controls^[70,71].

CONCLUSIONS

Human colonic motor activity is quite a complex issue, still

only partly understood and investigated, due to anatomic and physiological difficulties. In recent years, however, some more data have been obtained, even in proximal segments. These data have helped in elucidating, although only in part, some pathophysiological mechanisms of chronic constipation, and especially of the STC subtype. Unfortunately, the heterogeneity of the populations under study (that however are probably best selected with respect to other subtypes of constipation) accounts for certain discrepancies in the interpretation of the pathophysiological results. In addition, we are still lacking the “why”, i.e. we need more knowledge about the basic abnormalities of this disorder (nerve and/or smooth muscle involvement), which are still elusive and controversial^[72-75], in order to gain a more oriented therapeutic approach to this disease process.

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