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EDITORIAL

Paediatric and adult colonic manometry: A tool to help unravel the pathophysiology of constipation

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Abstract

Colonic motility subserves large bowel functions, including absorption, storage, propulsion and defaecation. Colonic motor dysfunction remains the leading hypothesis to explain symptom generation in chronic constipation, a heterogeneous condition which is extremely prevalent in the general population, and has huge socioeconomic impact and individual suffering. Physiological testing plays a crucial role in patient management, as it is now accepted that symptom-based assessment, although important, is unsatisfactory as the sole means of directing therapy. Colonic manometry provides a direct method for studying motor activities of the large bowel, and this review provides a contemporary understanding of how this technique has enhanced our knowledge of normal colonic motor physiology, as well as helping to elucidate pathophysiological mechanisms underlying constipation. Methodological approaches, including available catheter types, placement technique and recording protocols, are covered, along with a detailed description of recorded colonic motor activities. This review also critically examines the role of colonic manometry in current clinical practice, and how manometric assessment may aid diagnosis, classification and guide therapeutic intervention in the constipated individual. Most importantly, this review considers both adult and paediatric patients. Limitations of the procedure and a look to the future are also addressed.

Key words: Colon; Constipation; Manometry; Paediatric; Adult

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INTRODUCTION

Constipation is a common condition, with approximately 15% of adults and 9% of children reporting symptoms[1-4]. The direct and indirect costs are substantial; in the USA alone, an estimated $US1.7 billion/year is spent on adults[5] and a further $US3.9 billion/year on childhood constipation[6]. While anatomical malformation (e.g. anal stenosis, imperforate anus), metabolic and gastrointestinal causes (e.g. hypothyroidism, celiac disease, and cystic fibrosis),

intestinal nerve or muscle disorders (e.g. Hirschsprung disease, chronic idiopathic intestinal pseudo-obstruction), childbirth or pelvic surgery are known to cause constipation, for many patients, their condition is regarded as "idiopathic". Indeed, in children, it has been reported that less than 10% of those suffering from constipation have a recognizable underlying organic cause[7,8]. Defects in the nerves and pacemaker cells (e.g. decreased ICC density[9]) could be responsible in a proportion of cases, but as yet, techniques are not sufficiently developed to clearly identify such altered morphology, rendering any attribution to patho-aetiological significance (cause, effect, or epiphenomenon) speculative[8,10,11].

Given that both aetiology and pathophysiology are unclear in many cases, it is perhaps therefore not surprising that up to one-third of adults and children who seek medical help will fail non-surgical therapy[12,13]. Patients refractory to such interventions are debilitated, with physical functioning, mental health, general health and bodily pain all scoring poorly on quality of life questionnaires, compared to the non-constipated population[14]; indeed, the impact is comparable to other chronic conditions, such as inflammatory bowel disease in adults[15] and cancer in children[16]. In refractory cases, surgery, including subtotal or total colectomy, repair of anatomical anomalies believed to impede defaecation[17,18], appendicostomies[19], and more recently sacral nerve stimulation[20] may be considered. However surgical procedures are not without risk, with reported post-operative morbidity often high, and functional outcomes suboptimal[17,21,22]; this, in turn, equates to poor quality of life[23].

Improving therapies for functional bowel disorders is a fundamental goal for all researchers and clinicians working in this field, and to achieve this objective, a better understanding of pathophysiologies that may underpin such disorders is essential. In chronic constipation, altered colonic motor function remains the leading hypothesis to explain symptom generation, and this may be true not only for constipation associated with delayed colonic transit[24], but also for constipation allied to an evacuatory disorder[25]. In clinical practice, routine investigation of colonic motor function is achieved by use of transit studies (typically radio-opaque markers[24,26]), while defecatory function typically is assessed using evacuation proctography or balloon expulsion. Diagnostic manometry, which provides a direct assessment of those contractile activities subserving intestinal functions, is well developed for other parts of the gastrointestinal (GI) tract, notably the oesophagus and anorectum, but its diagnostic potential in the colon remains less certain. This is due to a number of factors including the relative inaccessibility of the proximal large bowel, the technical constrains of current manometric recording systems, and inadequate understanding of normal colonic motor physiology, which is fundamental to confidently diagnosing motor abnormalities in disease states. This review examines the equipment and protocols used to record colonic motor patterns *in vivo* in humans, with particular focus on the diagnostic relevance of data obtained, and the ability of colonic manometry to guide treatment. Current limitations and future direction for the procedure are also covered.

COLONIC MANOMETRY

Manometric studies of true colonic (as opposed to recto-sigmoid) motor function have been reported upon since the late 1980s[27]. However, the colon remains the least well understood section of the GI tract, particularly its proximal portions. For constipation, around 20 studies in adults, and fewer in paediatric populations, have been published. As such, colonic manometry is still largely used as a research tool in adults, with relatively few authors advocating diagnostic use[28,29]. Nevertheless, a recent American Neurogastroenterology and Motility Society consensus statement has recommended this test for the assessment of severely constipated patients (both adult and paediatric) who are unresponsive to medical therapy, and who have evidence of slow colonic transit in the absence of an evacuatory disorder[30]. Furthermore, in children, colonic manometry has been proposed to discriminate normal colonic motility from colonic neuromuscular disorders[31]. It may also help to clarify the pathophysiology of persistent lower GI symptoms after surgery for Hirschsprung disease, evaluate colonic involvement in a child diagnosed with idiopathic intestinal pseudo-obstruction syndrome, assess function of a diverted colon prior to possible re-anastomosis, and to assess colonic motor activity prior to intestinal transplantation to determine if the colon should be kept at the time of transplant[32]. What is certainly true is that colonic manometric procedures lack standardisation, with a variety of catheter types, placement techniques and protocols currently used.

It must also be remembered that colonic manometry is an invasive procedure, and as such should only be performed in those patients with symptoms severe enough to have a marked impact on their quality of life and social well-being. Extensive conventional treatment should be offered before testing colonic motility.

Catheter types

In general, there are two broad types of catheters used: (1) water-perfused; and (2) solid-state. As yet, there have been no studies which directly compare the two types. Preference for one over the other is guided by existing equipment, desired application, study design, and particularly cost.

Water-perfused manometry catheters: Water-perfused manometry is used in children and has been the preferred choice in the vast majority of studies in adults. Catheters are made of flexible PVC[27,33] or extruded lengths of silicone rubber[34]. The latter is highly flexible, and is desirable for patient tolerability if an oral route is used for intubation (see below). The catheters incorporate between 4 and 16 recording ports or side-holes, with an inter-side-hole distance of between 1 and 15 cm[24,35]. Each recording port

consists of an open lumen, which is connected to a pneumohydraulic infusion pump that ensures constant flow of water. The basic premise for recording is that contractions of the colonic wall occlude the manometric ports, thus impeding flow of perfusate (degassed water). Resistance to flow is transmitted as pressure change to external transducers, and the degree of resistance depends upon the amplitude and duration of the contraction. Such catheters are relatively inexpensive and highly versatile with regard to configuration (number, position and orientation of side-holes); in addition, silicone catheters are autoclaveable, and therefore can be re-used many times without fear of contamination. However, due to the requirement of being attached to the manometry system, and need for constant water infusion, studies are always performed in the laboratory setting. This confines the subject to a bed for the length of the recording period with minimal mobility allowed, thus creating a somewhat unphysiological environment. In addition, the volume of water introduced into the lumen is considerable (> 3 litres) if recording from multiple side-holes for prolonged periods of time. Whilst the colon does have the ability to absorb up to 6 litres of fluid a day[36], the effects of introduction of this amount of fluid upon colonic motility remains unknown.

Solid state manometry catheters: So-called 'solid-state' assemblies traditionally consist of strain gauges embedded into a flexible PVC catheter. Each strain gauge is attached to an amplification/recording system *via* fine connective wiring[35]. Until recently, solid-state catheters have typically had between 6 and 10 sensors spaced at 7-15 cm intervals[24]; however, recent technological advances now allow in excess of 20 sensors. Recorded pressure signals can be stored on portable digital recorders enabling the subject to be ambulant[29,37]. However, the cost of these catheters is considerable in comparison to water-perfused catheters, and there has been a tendency in the past for recording channels to break[38,39]. Nevertheless, with further technological improvements, and recent developments in fibre-optic technology, which has seen the emergence of an optical manometry system (see Future directions below), such limitations should be overcome[40,41].

Placement techniques

In human subjects, gaining access to the colon can generally be achieved through two routes: *antegrade* placement *via* the nose or mouth, or *retrograde* placement *via* the anus. Colonic catheters can alternatively be placed through a variety of stomas, a method used particularly in children[42-44] but also in adults[45].

Retrograde placement: This provides the easiest access to the colon, and is by far the most commonly used procedure in both adults and children[33,37,46,47]. In adults, catheters are placed with the aid of a colonoscope and can be positioned in the desired location. To date, most studies utilising this method have located the tip of the catheter at the hepatic flexure or mid-transverse colon, meaning that recordings are only achieved from sites distal to this. However, the Sydney group have achieved true pancolonic recordings over the past few years by securing the tip of the catheter to ascending colonic/caecal mucosal folds using endoclips[20,29,48,49]; this has the advantage of helping to prevent catheter displacement or excretion during defecation[50,51].

In children, the retrograde placement of colonic manometry catheters has also utilised colonoscopic procedures[46]; however, in recent years colonic catheters have also been successfully placed using fluoroscopic guidance alone, both through stomas and *via* the rectum[44]. However, this technique may be associated with prolonged exposure to radiation, in some cases up to 27 min[44].

One of the major advantages of retrograde catheter intubation is subject tolerability. Once the catheter has been sited, there is little or no discomfort. However, in addition to concerns over catheter displacement, there are other potential disadvantages, most notably the requirement for bowel preparation and usually some form of anaesthesia or sedation. The removal of faeces from the colon has recently been shown to result in an increase in the frequency of high amplitude propagating contractions[52,53], and also to disrupt the spatiotemporal organisation of propagating sequences (PSs)[53]. However, the colonic responses to physiological stimuli, such as a meal and morning waking, remain unchanged[53]. Nevertheless, it could be argued that bowel preparation is advantageous, in that the 'starting point' for each study, provided that bowel preparation is performed in an equivalent manner, is standardised.

Antegrade placement: This is a less common method for recording colonic motility and is restricted to adult studies[25,34,39,54]. The catheter is fed through the nasal cavity or mouth, and once through the pylorus (often achieved under fluoroscopic guidance), a balloon on the tip of the catheter is inflated with air or water to facilitate transit through the small and large bowel[25,34]. The main advantage of this procedure is that it obviates the need for bowel preparation, and thus the study is performed under essentially normal basal physiological conditions. The procedure is, however, time-consuming in comparison to retrograde catheter placement. Even in healthy controls, it may take up to 36 h to intubate the distal descending colon[34,35]. Furthermore, with the catheter *in situ* for a prolonged period of time, subject tolerability becomes an issue with nasal/oral/pharyngeal discomfort and nausea commonly reported. Finally, while antegrade placement can be used to study colonic motility in health and in patients with relatively normal colonic transit[25], its use in patients with slow transit constipation (STC) is problematic. As antegrade catheter placement relies on peristalsis to promote the catheter tip through the gut, the process can be greatly prolonged in patients with a disorder characterised by delayed gut transit (the primary clinical indication for this investigation[30]), especially when small bowel motility may also be also abnormal[55].

Placement through a stoma: Intubation *via* appendicostomy, caecostomy, ileostomy or colostomy has been used to successfully investigate children with STC[19,44,56]. In such subjects, after a preceding colonic washout, the in-dwelling device (e.g. Chait caecostomy button) is removed. Two techniques can then be adapted: (1) following sedation, the catheter can be advanced through the stoma with the aid of a guidewire, and positioned under fluoroscopic guidance[44]; and (2) a 10F feeding tube can be positioned through the stoma through which a Bisacodyl solution (2-4 mg) can be instilled directly into the caecum. A manometry catheter can then be introduced through the feeding tube and advanced in an antegrade direction along the colon. The Bisacodyl induces propulsive activity, and a balloon on the tip of the catheter can be inflated with water to aid propulsion through the large bowel[42,43].

RECORDED COLONIC MOTOR ACTIVITIES

Non-propagating motor activity

Non-propagating activity makes up the majority of a colonic manometric recording, consisting of apparently random pressure waves recorded at single or multiple recording sites, often alternating with phases of motor quiescence. Pressure waves may be sub-classified on the basis of duration, and are considered to be of either long duration (the majority) or short duration (often superimposed on long duration pressure waves). The presence of two types of phasic contraction in the colon is unique, compared with the remainder of the GI tract[57]. The functionality of non-propagating activity is outlined below.

Propagating motor activity

Propagating pressure waves are categorised into PSs (also termed propagating contractions) and high amplitude PSs (HAPSs; also termed high amplitude propagating contractions; Figure 1); the latter are recognised as the motor correlate of mass intraluminal movement and are involved in defaecation (Figure 2)[59-62]. Both PSs and HAPSs can be further qualified by the terms antegrade (aboral) or retrograde (oral), depending upon the direction of propagation. However, criteria used to define these events are inconsistent[35]. A general classification includes an array of 3 or more pressure waves recorded from adjacent recording sites, with a trough to peak amplitude $\geqslant$ 5 mmHg per pressure wave, in which the conduction velocity between wave onsets is between 0.2 and 12 cm/s[34,50]. The definition of what constitutes a HAPS is based on a threshold value for amplitude of one or more of the component pressure waves[35]; this varies markedly in the literature from > 50 to 136 mmHg[34,50,63-67]. Consequently, the range of published frequencies is wide[35]; in many cases, the chosen threshold value appears to be arbitrary. Some, however, are based on proven functional characteristics[34].

PSs are identified throughout the large bowel, although they originate with greater frequency in the proximal compared to the distal colon[37,38,58,59,68,69]. The majority of ascending colonic PSs do not migrate beyond the splenic flexure, and conduction velocity of PSs increases as the PS moves distally from the proximal colon, as does the amplitude of the propagating pressure waves[50,58,59,70].

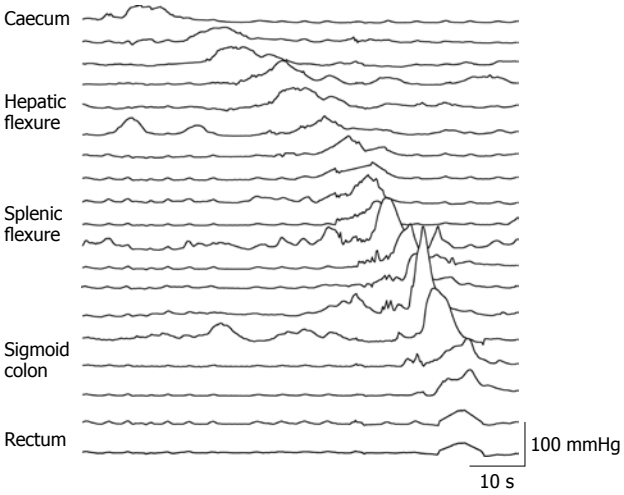

Figure 1 The high amplitude propagating sequence was first described in 1988[27]. The majority of these propagating events originate in the proximal colon and extend to the sigmoid colon. The amplitude of the component pressure waves increase as the motor patterns reaches the descending colon[58].

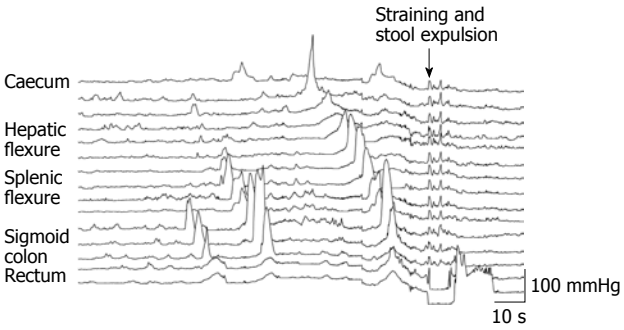

Figure 2 High amplitude propagating sequences are commonly associated with defaecation in healthy controls. Note the series of three high amplitude propagating sequences (HAPSs) prior to stool expulsion. The first originates at the distal descending colon, and with each subsequent HAPS, the site of origin moves to a more proximal location with the final HAPS extending the entire length of the colon[34].

Given their functional significance, HAPSs have garnered most interest in terms of pathological implication, and indeed decreased HAPS frequency is widely accepted as one of the principal hallmarks of STC (see below[27,29]). However, focus on propagated pressure waves alone, as is the case in many published reports, has perhaps led to their clinical impact being over-stressed, particularly given that they occur only a minority of the time during a colonic manometric recording; the organisation of other, more common motor activities may be of similar (or even greater) importance.

Organised colonic motor patterns

Akin to the interdigestive migrating motor complex of the upper GI tract[71], the colon exhibits periodic bursts of regular phasic pressure wave activity, termed either colonic

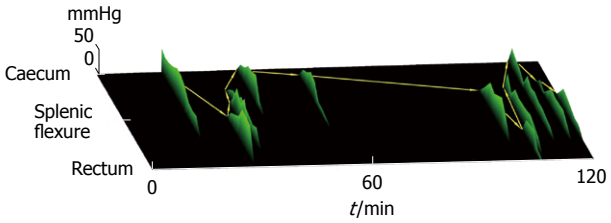

Figure 3 Two hour spatiotemporal maps of colonic propagating sequences in a female healthy control. In this map each individual ridge represents an antegrade propagating sequence. The start of each ridge indicates the site of origin and the time of day the propagating sequence occurred. The length of the ridge indicates the extent of propagation. The heights of the ridge indicate the amplitude of the component pressure waves. The yellow arrows link the site of origin of sequential propagating sequences. While no single propagating sequence spans the entire colon collectively, a linked series of propagating sequences can do so[76].

motor complexes[38,39,58] or rectal motor complexes (MC)[35,72], depending upon their site of origin. MCs predominate in the sigmoid or rectum, where they have also been termed "periodic rectal motor activity"[37,73,74]. The functional significance of these events is unclear, although it has been suggested that they provide a "brake" around the rectosigmoid junction[73], and reflect enteric neuromotor integrity, given that they occur in extrinsically denervated colon preparations[75].

In addition to MCs, sequential PSs have been shown to be linked in organized spatiotemporal patterns throughout the colon[76]. Many of these PSs form series in which three or more consecutive PSs demonstrate a regional shift in the colonic region from which they originate, i.e. each PS in a linked series will originate in a progressively more proximal or distal colonic location. Whilst most single PSs do not span the length the colon, collectively, a series of linked PSs can do so. It is likely that such linkage is important for the transport of content over longer lengths of the colon (Figure 3)[76].

COLONIC MANOMETRY PROTOCOLS

Paediatric studies

Despite the variety of placement techniques and catheter types, once the catheter is positioned, there is commonality to the actual recording protocol. In children, clinical studies generally do not last more than 4-5 h[77], but 24 h studies have been used in the research setting to provide more detailed information on motility characteristics[42,43]. Paediatric colonic manometry catheters typically contain 6-8 recording side holes, evenly spaced at 7.5, 10 or 15 cm intervals[42,43,77]. The paediatric colonic motility test includes at least 1 h of fasting and 1 h postprandial after finishing a high calorie meal. During the test, the child is required to remain in bed and it is important to have a trained observer at the bedside. If HAPSs are not recorded during the fasted or postprandial period, then drug stimulation with Bisacodyl (0.2 mg/kg, max 10 mg, diluted with 0.9% NaCl) is administered. HAPSs induced by Bisacodyl usually occur within a few minutes and are identical to spontaneous HAPSs. A cramping sensation and the urge to defaecate often accompany the presence of HAPSs[47]. If the paediatric test extends to 24 h, then the nocturnal frequency of motor patterns and the colonic response to waking are also measured[42,43,77].

Adult studies

In published adult colonic manometry studies, similar protocols are followed, although the catheter length is generally longer, containing up 16 sensors (water-perfused) spaced at 7.5 cm intervals[25,34]. Recordings are typically of 24 h duration. All studies examine two or more of the following: (1) fasting; (2) meal responses; (3) nocturnal suppression; (4) morning waking; and (5) response to chemical stimuli[24,35].

Normative data

For a clinical diagnosis, data collected from patients is compared to that obtained from healthy controls. In the adult population, recruitment of volunteers is generally not problematic, allowing normal ranges to be developed for various parameters of the motility recording (though it must again be stated that the size of published normative data sets remains inadequate).

By contrast, colonic motility recordings in truly healthy paediatric control subjects are lacking for obvious ethical reasons. Di Lorenzo *et al*[78] attempted colonic manometry in 32 "healthy" paediatric patients, though they were not strictly healthy controls, as they had diagnoses ranging from functional faecal retention (n = 15) and non-ulcer dyspepsia (n = 10), to Munchausen by proxy (n = 7). Other paediatric studies in adolescents with STC have used healthy young adults as the control group; whether this is appropriate is unknown[42,43].

OBSERVATIONS FROM COLONIC MANOMETRY STUDIES

Both propagating and non-propagating motor patterns may be temporally associated with propulsion and mixing of colonic content[59,60,79], signifying that these are important determinants of normal physiology in health and of pathophysiology in patient groups. In adult and paediatric patients with chronic constipation, a number of findings have been made which suggest pathological significance, including: (1) a lack of the normal[37,58,80] increase in colonic motor activity after a high calorie meal[29,43,46,49,80-86] (Figure 4); (2) a lack of the normal[29,50,51,58] suppression of colonic motor activity at night, and a suppressed or absent increase in colonic activity in response to morning waking[25,29,43,80] (Figure 4); (3) a decrease in frequency of HAPSs[27-29,39,47,49,80,83,85-88], although normal daily frequencies have also been reported in some constipated subjects[25,43] (Figure 4); (4) increased non-propagating activity in the left colon[89]; (5) absence[25] of the characteristic spatiotemporal patterning of PSs preceding normal spontaneous defecation[34]; (6) diminished co-ordination between

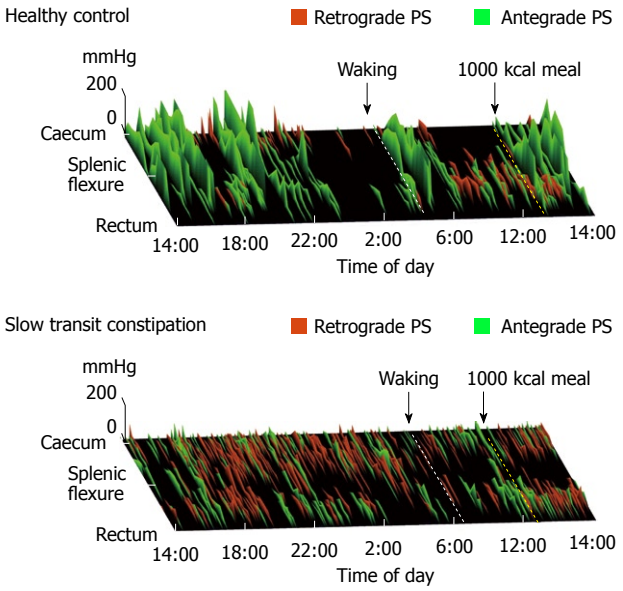

Figure 4 Twenty-four hour spatiotemporal maps[80] of colonic propagating sequences in a female healthy control and a female patient with slow transit constipation. Within each map the ridges represent antegrade (green) and retrograde (red) propagating sequences (PS). The antegrade PSs originate at the orad end of the green ridge and retrograde PSs originate at the anal end of the red ridges. The start of each antegrade and retrograde ridge indicates the site of origin and the time of day the PS occurred. The length of the ridge indicates the extent of propagation. The height of the ridge indicates the amplitude of the component pressure waves. The yellow-hatched line indicates when the 1000 kcal lunch was given, the white-hatched line indicates the time of morning waking. In health the frequency of propagating sequences are reduced during sleep and increase upon morning waking and in response to a high calorie meal. The map in the STC patients is characterized by an increased frequency of short extent PSs and a lack of high amplitude propagating sequences. There is an absent meal response (no increase in PSs) and an absent nocturnal suppression of PSs.

sequential pan-colonic PSs[76,80]; (7) a blunting of the normal[49] increase in PS or HAPS frequency in response to rectal or colonic infusion of Bisacodyl has been shown in a proportion of individuals[47,49,85], although in the majority of patients a normal response is recorded[49,83,85,90-92]; (8) a blunting of the normal increase in colonic HAPS frequency to intravenous injection of the cholinergic agonist edrophonium chloride[92]; (9) a blunting of the normal proximal colonic increase in motor activity in response to a rectal infusion of chenodeoxycholic acid[93]; (10) an increase in the frequency of HAPSs in response to sacral nerve stimulation in patients with STC[20]; and (11) a significant increase in the frequency of rectosigmoid motor complex activity[73,74].

CAN COLONIC MANOMETRY FINDINGS HELP TO DISTINGUISH SUBTYPES OF CONSTIPATION?

Constipation can be conceptualized into two broad overlapping categories: STC, and disorders of evacuation[1,94-96]. In some cases, this distinction among subgroups, based on aberrant physiological measurement, has proven beneficial in planning treatment and in predicting therapeutic outcome[96-99]. For example, identification of dyssynergic defaecation by anorectal manometry and balloon expulsion testing, in the absence of delayed colonic transit, is predictive of a high success rate from biofeedback[97,98]. Likewise, in carefully selected patients with severe STC, where the transit delay is restricted to the colon[17,22,100,101], and there is no evidence of evacuatory dysfunction, surgery such as colectomy with ileorectal anastomosis may be effective. In children this group is successfully managed with an appendix stoma and antegrade enemas[19].

In terms of colonic manometric investigation, specific biomarkers or biosignatures that may help to define constipation subtypes (and thus provide therapeutic targets) have, as yet, not been fully established. In adults, only three studies have addressed the validity of manometric findings between "recognised" subgroups[102-104]. The first concluded that intraluminal measurements could not be used to discriminate between subgroups of patients with either STC or an evacuation disorder[102]. The second study examined three subgroups of constipated patients with either STC, an evacuation disorder, or 'normal transit' constipation, and found that fasting and postprandial motor parameters were not useful for discriminating amongst these subtypes, although colonic compliance was[103]. Bassotti *et al*[104] noted that no colonic motor patterns were able to differentiate between constipated patients with or without delayed transit.

A further study in patients with constipation secondary to antidepressants revealed minimal motility differences compared to patients with idiopathic constipation[85]. Finally, Hervé *et al*[83] took the approach that manometric findings themselves should be used as the basis for subclassification. In a study of 40 adults with STC, they identified 4 subgroups: group 1 displayed no HAPS or a colonic response to a high calorie meal; group 2 showed increased sigmoid motor activity; group 3 had a reduced frequency of HAPSs; and group 4 displayed normal colonic motility. However the clinical impact of such findings, in terms of guiding successful management, remained undetermined. Nevertheless, through sufficiently large scale studies, a classification system incorporating findings from pancolonic manometric investigations, rather than being based on traditional studies of colonic transit and evacuatory function alone, may be merited. Current stratification, where the colon is seen to be responsible for transit, and the anorectum solely responsible for evacuation, is likely a gross oversimplification.

CAN COLONIC MANOMETRY HELP TO GUIDE TREATMENT AND IMPROVE OUTCOMES?

The primary indicators of abnormal colonic motor function in constipation (see above) are reduced HAPS frequency and a diminished or absent response to eating, morning waking or chemical stimulation. The colonic re-

sponse to ingestion of a meal is likely to involve the CNS and neurohormonal pathways; a suppressed response has been proposed as indicative of colonic myopathy and an absent response as a possible neuropathy[29]. Similarly, diurnal variation in colonic motor activity is likely to be mediated by the CNS, and therefore a diminished or absent response to sleep or morning waking supports a neuropathic cause in such patients[29]. With regard to chemical stimuli, a failed response may indicate an abnormality within the myenteric plexus[105], cholinergic pathways[92] or recto-colonic neural pathways[93].

Adult studies

In adults, very few interventional studies have been based upon evidence gained from colonic manometric investigation. In 3 patients with severe constipation who had failed conservative therapy, Bassotti *et al*[28] demonstrated globally reduced colonic motility, a minimal meal response and no response to Edrophonium. Based upon these data, 2 patients underwent a total colectomy and 1 a hemicolectomy, with "fairly good results at follow-up" reported. No long-term data were provided.

In a larger study, Rao *et al*[29] performed 24 h colonic manometry in 21 patients with STC. Utilising the response to ingestion of a meal, response to morning waking, and HAPS frequency as diagnostic criteria, patients were classified as having a neuropathy (n = 10) if they had an absence of two or more, a myopathy (n = 5) if they had a reduced response to two or more, or being normal (n = 6). Those with a suspected neuropathy were offered a colectomy (performed in 7/10, with "improved" bowel symptoms reported; no follow-up duration specified). Those with a myopathy were offered a regime of biofeedback and laxatives, and reported "modest improvement" at 1 year.

Paediatric studies

In children, colonic manometry studies are far more likely to guide treatment options. In a study by Pensabene *et al*[106], results of colonic manometry testing resulted in a recommendation to change therapy (mostly surgical) in 93% of the patients with intractable organic or functional constipation. Importantly, 88% of the 98 parents believed that the therapeutic suggestions made had been helpful in improving their child's health[106].

Di Lorenzo *et al*[107] studied 46 children with constipation and/or faecal incontinence after surgery for Hirschsprung disease. Four groups were established based upon results from colonic manometry: (1) HAPSs propagating from the proximal colon through the neorectum to the anal sphincter, which was associated with faecal incontinence (n = 18); (2) an absence of HAPSs and lack of colonic meal response, which was predominantly associated with constipation (n = 15); (3) a normal manometric study, with a hypertensive anal sphincter, which was invariably associated with constipation (n = 4); and (4) a normal manometric study, but the child presented with fear of defaecation and retentive posturing, which was predominantly associated with constipation and soiling (n = 9). Those in group one were treated with anticholinergics and Loperamide. In group two, resection of the abnormal section of colon was recommended. In the third group, four-quadrant intrasphincteric botulinum toxin injections were recommended, and in the fourth group, a programme of behaviour modification and stool softeners were used[107]. Based upon these treatments, the authors reported an improvement in global health and emotional health scores as well as an improvement in the number of bowel movements and resolution of abdominal pain[107].

Also in paediatric patients, colonic manometry is reported to have value in determining poor outcomes for the surgical treatment of intractable constipation using an appendicostomy or a caecostomy with antegrade irrigation of the colon[47]. For example, those children with a poor outcome also displayed an absence of colonic response to Bisacodyl. However, the fact that 50% of children with no production of HAPS still had good outcomes to antegrade irrigation suggests that the Bisacodyl response is by no means a solid predictor[47].

CURRENT LIMITATIONS

While colonic manometry studies in both children and adults have helped to define some of the physiological and pathophysiological aspects of colonic motor function, there are still no published quantitative data on propagating or non-propagating activity that clearly differentiates healthy subjects from constipated patients[30]. Furthermore, at least in children, morphological changes reflecting possible myogenic or neurogenic disorders in muscle tissue do not correlate with particular features of colonic manometric recordings[108] or anorectal manometry[109]. It also remains unclear whether data derived from adult studies can be extrapolated to children and *vice versa*. No manometric studies using the same equipment and protocols have compared childhood and adult constipation. Indeed, because a normal frequency of HAPSs has been identified in children with STC (contradicting most reported findings in adults), childhood constipation may represent a different entity[43]. The impact of sensory, as opposed to motor dysfunction on the development of constipation is gaining increasing recognition[110,111]. Nevertheless, the two are inextricably linked, and future studies should look to explore both domains concurrently, by the best methods available, rather than consider certain functional bowel conditions as principally motor disorders (e.g. constipation), and others as sensory disorders (e.g. the irritable bowel syndrome).

With variations in protocols, catheter types, numbers of recording sites, spacing between recording sites, placement techniques and definitions of recorded activities, it is perhaps not surprising that consistent findings have not been reported in the literature[24,35]. Furthermore (and as stated above[24]), almost all studies that detail "colonic" manometry have, in reality, recorded colonic motor patterns distal to the mid-transverse colon. Support for the use of true pancolonic manometry resides in the fact that

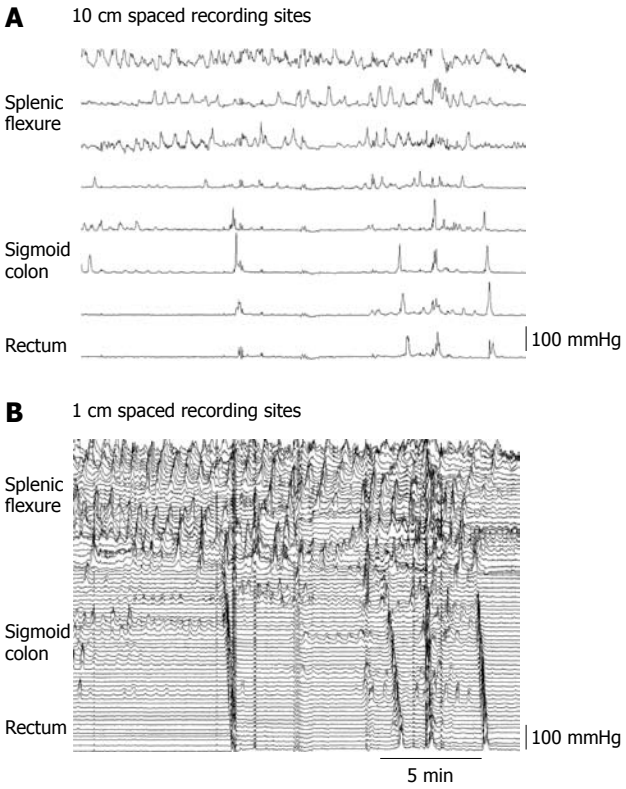

Figure 5 Manometric traces of colonic motor activity recorded by a fibre-optic manometry catheter with 90 sensors spaced at 1 cm intervals. A: To represent common sensor spacing for current published colonic recordings, the data set, obtained through "high resolution" manometry, is sub-sampled to present every 10th channel (10 cm spacing, top); B: The complete data set, captured at 1 cm intervals, is displayed at the bottom. Note that at 10 cm spacing, the most proximal three channels reveal what appears to be non-propagating pressure waves. However, when the full data set is viewed (B), a series of short-extent retrograde propagating events are detected. These events are missed when spatial resolution is poor. Modified from[41].

PS and HAPS are not distributed evenly throughout the colon, and predominantly originate in the ascending and proximal transverse colon, and that the entire colon appears to function in a coordinated fashion[76,112]. 'Partial' colonic recordings thus provide an incomplete picture of colonic (patho)physiology.

FUTURE DIRECTIONS

In the oesophagus and the anorectum, manometry is an established diagnostic tool. In comparison to the colon, these regions afford easier access and therefore have been subjected to far more research and clinical investigation. More recently, development of high resolution manometry (HRM) has further enhanced diagnostic potential, particularly in the oesophagus[113], most notably with regard to standardisation of recording procedures. With the advent of fibre-optic manometry[40,114], HRM recordings are now feasible throughout the entire colon. Catheters incorporating up to 120 sensors spaced at 1 cm intervals have already demonstrated that the vast majority of PSs propagating over short distances are missed by recording sites spaced > 7 cm apart[40,41] (Figure 5). If such technology is able to identify those elusive biomarkers that can help to reliably distinguish constipation subtypes and guide management, then this provides the opportunity to take colonic manometry out of the research arena and into clinical practice. Such progress is only possible through appropriately designed and powered studies, utilising equivalent hardware and software, both in adults and children. The revolution that has been seen with oesophageal HRM, such that traditional manometry is now regarded as obsolete, can serve as a template for the clinical potential of pancolonic manometric investigation.

CONCLUSION

Pancolonic manometric investigation provides a unique window onto motor functions of the large bowel, and through its use we now have a greater understanding of normal colonic physiology and also the pathophysiology of constipation in both adults and children. Although a recent consensus statement[30] advocates use of colonic manometry in patients with "significant motility disorders", the technique is still not refined enough for widespread clinical use, and no prospective and controlled studies have been performed evaluating the clinical value of this tool. Nevertheless, technological advances offer the potential of adding colonic manometry to the available diagnostic armamentarium in broader clinical practice. To achieve such a goal, there is a fundamental requirement for standardisation of methodologies and recording protocols, further development of automated analysis software, and a vital need for generating larger normative data sets, which will enable diagnostic yield to improve. This will be achieved through the coordinated efforts of those dedicated to this field. Further clinical exploration of this technique affords the possibility of a more directed therapeutic approach in patients with chronic constipation. Colonic manometric studies, performed in large numbers of constipated patients, will hopefully establish biomarkers that can distinguish existing (largely predetermined) constipation subtypes (i.e. STC, evacuation disorders), or aid a more contemporary phenotypic classification.

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