Regional Gastrointestinal Motility in Healthy Children

Brinck, Christian Emil; Mark, Esben Bolvig; Ejerskov, Cecilie; Johansen, Klaus Birkelund; Sutter, Nanna; Schlageter, Vincent; Drewes, Asbjørn Mohr; Krogh, Klaus

Published in:
Journal of Pediatric Gastroenterology and Nutrition

DOI (link to publication from Publisher):
10.1097/MPG.0000000000003198

Publication date:
2021

Document Version
Accepted author manuscript, peer reviewed version

Journal of Pediatric Gastroenterology and Nutrition, Publish Ahead of Print

DOI : 10.1097/MPG.0000000000003198

Regional Gastrointestinal Motility in Healthy Children

Christian Emil **Brinck**, BS[1, 2], Esben Bolvig **Mark**, PhD[3], Cecilie **Ejerskov** PhD[1], Klaus Birkelund **Johansen**, MD[1], Nanna **Sutter**, MD[2], Vincent **Schlageter**, PhD[4], Asbjørn Mohr **Drewes**, DMSc[3], Klaus **Krogh**, DMSc[2]

1: Department of Pediatrics and Adolescent Medicine, Aarhus University Hospital, Aarhus, Denmark

2: Department of Hepatology and Gastroenterology, Aarhus University Hospital, Aarhus, Denmark

3: Mech-Sense, Department of Gastroenterology and Hepatology, Aalborg University Hospital, Aalborg, Denmark

4: Motilis Medica SA, Lausanne, Switzerland

Corresponding author

Christian Emil Brinck

Department of Pediatrics and Adolescent Medicine, Aarhus University Hospital

Palle Juul-Jensens Boulevard 99, 8200 Aarhus N, Denmark

Email: ceb@clin.au.dk; Telephone: +45 2711 0447

Conflict of Interest and Source of Funding

VS is co-owner of Motilis Medica SA. VS contributed with technical information for the protocols for the Danish Ethics Committee and the Danish Medicines Agency. During the study he was solely involved when technical issues arose with the equipment. All other authors have no conflicts of interest to disclose.

This publication was partly funded by The Danish Children's Cancer Foundation, Denmark (grant number 20183919 to CEB); The Louis-Hansen Foundation, Denmark (grant number 192B4547 to CEB); The Ronald McDonald Children's Foundation, Denmark (*no grant number* to CEB).

Clinical Trial Registration

The trial is registered at ClinicalTrials.gov. ID: NCT03981510

https://www.clinicaltrials.gov/ct2/show/NCT03981510?term=NCT03981510&draw=2&rank=1

Abstract

Objective: To evaluate the safety and use of the 3D-Transit system (Motilis SA, Lausanne, Switzerland) **and** to describe regional gastrointestinal transit times, segmental colonic transit times and colonic movement patterns in healthy children. **Methods:** 21 healthy children (11 girls, median age 10.5 years, range 7-15 years) were included. For evaluation of gastrointestinal transit times and colonic movement patterns, we used the minimally-invasive electromagnetic 3D-Transit system. A small electromagnetic capsule (21.5 x 8.3 mm) was ingested and tracked through the gastrointestinal tract by a body-worn detector. Regional gastrointestinal transit times were assessed as time between capsule passage of anatomical landmarks. Colonic movement patterns were described and classified based on capsule movement velocity, direction, and distance. **Results:** One child could not swallow the capsule and 20 children completed the study without any discomfort or side-effects. Median whole gut transit time was 33.6 (range 10.7–80.5) hours, median gastric emptying time was 1.9 (range 0.1–22.1) hours, median small intestinal transit time was 4.9 (range 1.1–15.1) hours, and median colonic transit time was 26.4 (range 6.8–74.5) hours. Median ascending colon/cecum transit time was 9.7 (range 0.3–48.1) hours, median transverse colon transit time was 5.6 (range 0.0–11.6) hours, median descending colon transit time was 2.6 (range 0.01–22.3) hours, and median sigmoid colon/rectum transit time was 7.5 (range 0.1–31.6) hours. Colonic movement patterns among children corresponded to those previously described in healthy adults.

Conclusions: The 3D-Transit system is a well-tolerated and minimally-invasive method for assessment of gastrointestinal motility in children.

Key Words: electromagnetic tracking, gastric emptying, small intestinal transit time, colonic transit time, colonic movement patterns

What is known?

- Gastrointestinal (GI) motility disorders in children represent a challenging task for pediatricians.
- Assessment of regional GI transit times may be important for understanding gastrointestinal symptoms in children.
- Data on GI transit times in children are very limited.

What is new?

- The 3D-Transit system is well-tolerated and without any side-effects in healthy children.

- The 3D-Transit system enables assessment of regional GI transit times in healthy children aged 7–17 years.

List of abbreviations:

GI = gastrointestinal

ROM = radiopaque markers

BMI = body mass index

MTS-1 = motility tracking system 1

WMC = wireless motility capsule

CPM = contractions per minute

Introduction

Disorders of gastrointestinal (GI) motility in children, such as functional constipation, fecal incontinence, gastroesophageal reflux, and irritable bowel syndrome represent an important problem with a prevalence of nearly 25% in otherwise healthy children (1, 2). The prevalence is as high as 80%–90% in children with neurological impairment (3). Symptoms include constipation, diarrhea, vomiting, dysphagia, abdominal pain, and abdominal bloating. They cause a considerable decrease in health-related quality of life and often persist into adulthood despite medical treatment (4-6).

Gastrointestinal dysmotility causes either delayed or accelerated transit through the stomach, small intestine or colon. Direct assessment of regional transit times is important for clinicians when evaluating the underlying causes and planning therapy. However, currently available methods, such as radiopaque markers (ROM), scintigraphy, and colonic manometry hold inherent limitations, especially in children (7-9). Consequently, the understanding of both normative GI motility and the underlying pathophysiological mechanisms of GI dysmotility in children are sparse (10).

The 3D-transit system (Motilis, Lausanne, Switzerland) enables continuous measurement throughout the GI tract, which provides assessment of both regional GI transit times, whole gut transit time, segmental colonic transit times, and colonic movement patterns (11-13). The system features an electromagnetic capsule and a portable body-worn detector which in adults enables measurements in the home environment under near-normal physiological conditions (14). The system has not yet been used in children.

Our aims were to evaluate the safety and performance of 3D-Transit and to describe regional GI transit times, segmental colonic transit times, and colonic movement patterns in healthy children aged 7-17 years. We hypothesized that the 3D-Transit system could provide data on GI motility without any discomfort or safety issues and that the transit patterns previously described in adults were present in children too.

Methods

The study was a descriptive cohort study conducted at the Department of Hepatology and Gastroenterology, Aarhus University Hospital, Denmark. We recruited children through public advertising and by direct inclusion. Children were eligible if they were 7–17 years, were without GI symptoms, and if both child and parents were capable of understanding the given information. Exclusion criteria included known disorders of the GI tract, previous neurological or GI surgery, current use of medication affecting GI function, known difficulties with swallowing, or any known stricture, perforation, or obstruction of the GI tract. Informed oral and written consent were obtained from both parents for each child. Children aged 15–17 years also gave oral consent based on age-levelled written information.

The study was conducted according to the Helsinki Declaration II, approved by the Danish Medicines Agency (Project ID 2019032399), monitored by the Good Clinical Practice Unit, Aarhus University Hospital, Denmark (EUDAMED CIV-ID 1903027684), approved by the local Ethical Committee (Project ID 110724419), and registered at ClinicalTrials.gov (ID: NCT03981510).

Study endpoints

The primary endpoint was to evaluate the 3D-Transit system as a safe and well-tolerated method in children. Secondary endpoints included assessment of 1) regional and total GI transit times, 2) segmental colonic transit times and 3) colonic movement patterns, and 4) influence of age and gender on regional GI transit times.

Study protocol

The study included three visits. 1) The child and the parents were orally and in writing informed about the study and the eligibility criteria were evaluated. 2) The child came in the morning, fasting for at least 6 hours, and received a standardized breakfast meal (a granola bar, 99 kcal). A capsule was ingested with a glass of water. To ensure the return of fasting motor activity of the stomach, the child was instructed to wait 4 hours from time of capsule ingestion until the next meal. Shortly after capsule ingestion, the child was sent home to proceed with normal daily activities with only minor limitations on heavy physical body movements, such as running, cycling, jumping etc. The investigation was completed when the capsule was expelled, as monitored by the computer software 48 hours after ingestion of the capsule. Another visit was scheduled after 72 hours (and 96 hours etc.) if the capsule still resided the GI tract.

While under study, the child was instructed to keep a diary noting time of bowel movements, consistency of stools as measured on the Bristol stool scale, time of meals, and erroneous episodes of heavy physical body movements (15). The child was not restricted to any dietary control before or during the study.

Motilis 3D-Transit System

The 3D-Transit system consists of a portable detector plate located in a body-worn belt around the waist, a small electromagnetic capsule (size: 21.5 mm x 8.3 mm, density: 1.6 g/cm^2) and a computer with analysis software (see figure 1A). Each capsule contains a plastic-coated electromagnet with a sampling rate at 5 Hz and a battery with a lifetime of approximately 98 hours. Physical movements are recorded by an accelerometer located inside the detector. Breathing movements are recorded by a chest-worn respiratory belt (12). Data are stored on a SD-card in the detector and subsequently transferred to a computer for analysis.

3D-Transit data analysis

All data analysis was conducted manually by investigators CEB, NS, and EBM.

Regional gastrointestinal transit times

Analysis of regional GI transit times was performed using dedicated software (MTS Record, Motilis, Lausanne, Switzerland). To assess regional GI transit times, four anatomical landmarks were recognized by examination of the 2D-plot (capsule position, X and Y) and detection of changes in contraction frequencies (capsule orientation, θ and φ), as seen in figure 1A. The four anatomical landmarks were: 1) ingestion, 2) pyloric passage, 3) ileocecal passage, and 4) exit of the capsule. Gastric emptying time was defined as the time from 1) to 2), small intestinal transit time as time from 2) to 3), and colonic transit time as time from 3) to 4).

The overview function of the 3D-Transit software supported the evaluation of these transitions by displaying a heat map of contraction frequencies throughout the investigation (see figure 1B). Pyloric passage was characterized by a shift from three contractions per minute (cpm) (stomach) to 8-11 cpm (proximal small intestine), alongside the appearance of the duodenal arch in the 2D-plot (see figure 1C). Ileocecal passage was characterized by a shift from 6 cpm (distal ileum) to 3 cpm (colon), and the occurrence of a short fast movement in the lower right quadrant. Exit of the capsule was seen as a centered vertical drop on the 2D-plot followed by complete signal loss from the capsule, corresponding with time of a bowel movement noted in the diary (16).

Segmental colonic transit times and colonic movement patterns

The colon was divided into six segments: 1) caecum/ascending colon, 2) transverse colon, 3) descending colon, 4) rectosigmoid colon, 5) total right colon, and 6) total left colon. This was

done by assessment of six anatomical landmarks in the colon: (i) start of the colon, (ii) hepatic flexure, (iii) midpoint of the transverse segment, (iv) splenic flexure, (v) distal end of the descending colon, and (vi) distal limit of the rectum.

Colonic movement patterns were classified as five specific movement patterns in regard to capsule movement length, velocity, and direction: a) long fast antegrade movement (>10 cm and >10 cm/min), b) fast antegrade movement (<10 cm, >4 cm, and >4 cm/min), c) slow antegrade movement (>4 cm, <4 cm/min, and >4 cm/h), d) slow retrograde movement (<−4 cm, <4 cm/min, and >4 cm/h), and e) fast retrograde movement (<−4 cm and >4 cm/min). Long fast antegrade movements are similar to what is also named colonic mass movements in literature. The analysis process is described in greater detail by Mark et al. (11).

Statistical analysis and study power

Study data were collected and managed using REDCap (Vanderbuilt University, Nashville, TN, USA) electronic data capture tools hosted at Aarhus University Hospital (17, 18). All analyses were performed using STATA version 16 (StataCorp LP, College Station, TX, USA). GI transit times and colonic motility parameters were nonparametric and presented as median, range and the 5^{th} and 95^{th} percentile. Level of statistical significance was set at 0.05. Median number of stools per day was calculated as (total number of stools during capsule residence in the GI tract) / (whole gut transit time in hours) / (24 hours). A Spearman's correlation test was performed to evaluate correlation between stool consistency and frequency, and regional GI transit times. Linear regression analysis was performed to evaluate effect of age on all regional and segmental transit times. Non-parametric Mann-Whitney test was performed to evaluate difference in BMI and age between boys and girls, and to evaluate difference of gender on all regional GI transit times. The sample size of 20 children was thought to be adequate for the purpose of this descriptive study as previous similar studies have used comparable sample sizes (14, 19).

Results

Healthy children

A total of 21 healthy children (10 boys, mean age 10.8 years, range 7–15 years, mean BMI 18.1, range 15–24) met the criteria and were included in June–September 2020. One girl (10 years) was unable to swallow the capsule. The remaining 20 had no difficulties swallowing the capsule and all investigations were well-tolerated. There were no technical difficulties and no reported side-effects. There was no significant difference in age or BMI between boys and girls ($P = 0.54$ and $P = 0.44$).

Bowel movements

The median number of stools per day was 1.7 (range 0.8–4.5), and the median score on the Bristol stool scale was 4 (range 2–6). Bowel movements were distributed as follows: 16.9%

before 10 AM, 9.2% between 10 AM and 1 PM, 40.0% between 1 PM and 5 PM and 33.9% after 5 PM.

Gastrointestinal transit times

Median whole gut transit time was 33.6 (range 10.7–80.5) hours. Table 1 displays regional GI transit times and segmental colonic transit times for each subject. Median and range are presented for both genders, boys, and girls. There were no differences between boys and girls on gastric emptying time ($P = 0.63$), small intestinal transit time ($P = 0.63$), colonic transit time ($P = 0.91$), ascending colonic transit time ($P = 1.00$), or transverse colonic transit time ($P = 0.90$). Rectosigmoid transit time was significantly longer and descending colonic transit time was significantly shorter in girls compared to boys ($P = 0.04$ and $P = 0.03$). There were no effects of age on any of the regional GI transit times (all P-values > 0.38). There was a statistically significant inverse association between stool frequency and both rectosigmoid transit time ($P = 0.03$) and total left colonic transit time ($P = 0.01$). There was no correlation between stool frequency and the remaining regional and segmental colonic transit times (all P-values > 0.22). There was no significant correlation between stool consistency and any regional transit times (all P-values > 0.06) (see Table, Supplementary Digital Content 1, http://links.lww.com/MPG/C378, which shows the correlation between age, stool frequency, stool consistency, and all regional transit times).

Colonic movement patterns

The 3D-Transit system allowed for detailed description of individual colonic transit patterns (see Table 2). As shown in figure 2, two children with comparable colonic transit times within normal range, can represent two very different progression patterns in the colon. Figure 2A displays a steady colonic progression and a final long fast antegrade movement in the rectosigmoid segment simultaneous with a bowel movement. Contrarily, figure 2B displays a colonic progression with long periods of very slow or no progression followed by a singular long fast antegrade movement, which actually consists of two movements split by a six-minute pause. The first covers 44 cm in 1.5 min (ascending to mid descending colon) and the second 17 cm in 1.8 min (mid descending to mid-sigmoid).

Discussion

The present study shows that the 3D-Transit system can be used for description of GI motility in children aged 7–17 years. Accordingly, regional transit times, segmental colonic transit times, and colonic movement patterns were described in healthy children and were comparable in data quality to what has been previously observed in adults.

ROM have been used since the 1980's to assess colonic transit time in both healthy children and children with GI dysmotility (20-22). Mean colonic transit times reported in studies on healthy children range from 15.1 to 39.6 hours (20, 23-26). One study used ROM in children to find that stool consistency, but not frequency, correlated with colonic transit

time (22). We found a statistically significant inverse association between stool frequency and rectosigmoid transit time and total left colonic transit time. We did not find neither stool consistency to correlate with any regional transit time, possibly due to our relatively small sample size (n = 20).

ROM enable distinction of three segmental colonic transit times (left colon, right colon, rectosigmoid colon). However, the actual assessment is not colonic transit time, but essentially whole gut transit time as a mathematically calculated surrogate hereof. It is also debated whether the analysis method actually assign markers to incorrect colon segments and hence miscalculates the segmental colonic transit times (27). Most importantly the method does not provide any information on gastric emptying time, small intestinal transit time, or movement patterns of the GI tract. This is an essential drawback to the method as GI motility disorders often affect more than one region of the GI tract (28). A recent study with both healthy and constipated children validated a method using magnetic resonance imaging and small ingestible mini-capsules, thus avoiding radiation and improving image quality compared to X-ray and ROM (29).

Regional GI transit times have previously been assessed in 12 healthy children by using a pH-capsule (2.6 x 8 mm) (30). The authors found a median gastric emptying time of 1.1 (range 0.2–2.3) hours, median small intestinal transit time of 7.5 (range 5.1–9.2) hours, and median colonic transit time of 17.5 (range 6.2–54.7) hours. These transit times are numerically shorter than what we have found which may be explained by the small number of children and differences in methodologies.

The wireless motility capsule (WMC; SmartPill™, Medtronic, MN, USA) measures pH, temperature and pressure in order to assess regional GI transit times. However, the WMC does not enable assessment of segmental colonic transit times or colonic movement patterns, as it is possible with the 3D-Transit system. Another drawback of the potential use of WMC in pediatric research is the size of the ingestible capsule (26 x 13 mm), which is larger than the 3D-Transit capsule (21.5 x 8.3 mm). The WMC has recently been used in a study among 57 GI symptomatic children aged 8-17 (median 16) years (31). However, since no study has used WMC in healthy children, normative values remain unknown.

The precursor of the 3D-Transit system (MTS-1) has previously been successfully used to assess regional transit times in healthy children aged 7-12 years, with findings on regional GI transit times very similar to those of the present study (19). However, the MTS-1 uses a permanent magnetic capsule, which requires the subject to stay in a non-magnetic bed while under study. Therefore, recordings were not ambulatory or continuous and were limited to a duration of eight hours on the first day and four hours on the second day. The MTS-1 has not been used in clinical research since 2014.

In accordance with previous studies using the 3D-Transit system in adults, inter-subject variation among children was large. For instance, one girl (7 years) and one boy (13 years) with whole gut transit times in the normal range area had remarkably long gastric emptying

times (17.8 and 22.1 hours). This was despite both children being absolutely healthy and not eating until after the four-hour fasting period, as noted in the diaries kept under study. Ingesting a meal with the capsule still present in the stomach could potentially contribute to the prolonged gastric emptying time. Probably, the four-hour fasting period after capsule ingestion, which intended to allow pyloric passage of the capsule during a phase III of the migrating motor complex was not sufficient in these two children. Additionally, two children had remarkably slow transit through the whole gut (80.7 and 78.9 hours). In those cases, the capsule resided in the cecum for 73% and 42% of total colonic transit time, respectively. The heavily elongated transit of the two children may be attributed as physiological variance similar to previous findings in studies using ROM (23).

Normative data have been published from 111 3D-Transit examinations of healthy adults (32). Direct comparison to the present study is not possible due to variations in protocols. However, the pilot study on 20 healthy adults was performed at our unit following almost the same protocol as in the present study on children (14). Comparing data from the two studies, children had a significantly shorter gastric emptying time, but significantly longer colonic and whole gut transit times. This difference between children and adults may have numerous causes of both physiological and social origin. In contrast to data from healthy adults, we found that 74% of the children's bowel movements took place after 1PM. The colonic movement patterns presented in Table 2 are very similar to what has been found with the 3D-Transit system in healthy adults (n = 34) (11). One difference between these protocols was the size of the standardized meal, where adults were given two granola bars and children one (99 kcal). For comparison, studies with the WMC in both adults and children use the SmartBar® (255 kcal) (31, 33).

There are several limitations to the present study. General limitations to the 3D-Transit system include manual analysis, lack of availability, the non-direct measurement of GI contractions, and the minor restrictions in daily activities such as sports etc. while under study (12). Data loss is also generally described as a limitation but was not experienced as a problem in the present study. The primary limitation for this present study is the sample size of children. However, the primary outcome of this study was to evaluate the 3D-Transit system as a safe and well-tolerated method in children, to which the current sample size is adequate. A larger number of children would strengthen the study's power to evaluate the effect of age, and gender on any transit times, and help establish more robust normative values. Another potential limitation is the size and viscosity of the capsule, as the content passing from the ileum to the right colon is semi-fluid. Therefore, it might be a concern that indigestible solid particles, such as the 3D-Transit capsule or WMC, could behave differently from normal stools. For instance, two children in the study had very long gastric emptying times of 17.2 and 22.1 hours and we have no obvious explanation for this. The size of the test meal (99 kcal) was smaller than the one used in the pediatric WMC study (SmartBar®, 255 kcal). However, it is unlikely that this difference can explain the delayed gastric emptying. The risk of having very prolonged gastric emptying times in healthy children could probably be reduced by postponing the first meal after the intake

of the capsule. However, we also wanted to study the children under circumstances close to their daily habits and close to those used in previous studies with the system in adults. Finally, the study protocol should be acceptable to children as young as 7 years of age.

To ensure data quality, children were instructed to abstain from all heavy physical body movements while under study. Therefore, a potential concern would be that inactivity could affect GI motility. When only using one capsule, another limitation is inevitable as valuable information from segments where the capsule is not present could potentially be missed. This could have been accommodated by use of three capsules in 12-hour intervals, as permitted by the 3D-Transit system, or by use of the more invasive high-resolution colonic manometry, where pressure changes are directly measured contrary to the indirect measures of the 3D-Transit system. Only one study has validated the 3D-Transit system to ROM in adults. Future studies will need to look into this, together with validation of the 3D-Transit system with colonic manometry and the WMC. Finally, the 3D-Transit system needs FDA approval and CE marking.

Conclusion

In conclusion, the 3D-Transit system appears to be well tolerated in children as young as 7 years without any discomfort or safety issues. The system provides data on both regional GI transit times, segmental colonic transit times, and colonic movement patterns. It holds the potential for future research of GI motility in children with various GI disorders.

REFERENCES

1. Robin SG, Keller C, Zwiener R, et al. Prevalence of Pediatric Functional Gastrointestinal Disorders Utilizing the Rome IV Criteria. J Pediatr. 2018;195:134-9.

2. Saps M, Velasco-Benitez CA, Langshaw AH, et al. Prevalence of Functional Gastrointestinal Disorders in Children and Adolescents: Comparison Between Rome III and Rome IV Criteria. J Pediatr. 2018;199:212-6.

3. Quitadamo P, Thapar N, Staiano A, et al. Gastrointestinal and nutritional problems in neurologically impaired children. Eur J Paediatr Neurol. 2016;20(6):810-5.

4. Khan S, Campo J, Bridge JA, Cet al. Long-Term Outcome of Functional Childhood Constipation. Digestive Diseases and Sciences. 2007;52(1):64-9.

5. Bongers ME, Benninga MA, Maurice-Stam H, et al. Health-related quality of life in young adults with symptoms of constipation continuing from childhood into adulthood. Health Qual Life Outcomes. 2009;7:20.

6. Varni JW, Bendo CB, Nurko S, et al. Health-related quality of life in pediatric patients with functional and organic gastrointestinal diseases. J Pediatr. 2015;166(1):85-90.

7. Dinning PG, Smith TK, Scott SM. Pathophysiology of colonic causes of chronic constipation. Neurogastroenterol Motil. 2009;21 Suppl 2(Suppl 2):20-30.

8. Rosen R, Garza JM, Tipnis N, et al. An ANMS-NASPGHAN consensus document on esophageal and antroduodenal manometry in children. Neurogastroenterol Motil. 2018;30(3).

9. Rodriguez L, Sood M, Di Lorenzo C, et al. An ANMS-NASPGHAN consensus document on anorectal and colonic manometry in children. Neurogastroenterol Motil. 2017;29(1).

10. Bongers MEJ, Van Wijk MP, Reitsma JB, et al. Long-Term Prognosis for Childhood Constipation: Clinical Outcomes in Adulthood. 2010;126(1):e156-e62.

11. Mark EB, Poulsen JL, Haase A-M, et al. Ambulatory assessment of colonic motility using the electromagnetic capsule tracking system. Neurogastroenterol Motil 2019;31(2):e13451.

12. Brinck CE, Mark EB, Winther Klinge M, et al. Magnetic tracking of gastrointestinal motility. Physiol Meas. 2020.

13. Sutter N, Klinge MW, Mark EB, et al. Normative values for gastric motility assessed with the 3D-transit electromagnetic tracking system. Neurogastroenterol Motil 2020;32:e13829

14. Haase AM, Gregersen T, Schlageter V, et al. Pilot study trialling a new ambulatory method for the clinical assessment of regional gastrointestinal transit using multiple electromagnetic capsules. Neurogastroenterol Motil 2014;26(12):1783-91.

15. Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. Scand J Gastroenterol. 1997;32(9):920-4.

16. Worsøe J, Fynne L, Gregersen T, et al. Gastric transit and small intestinal transit time and motility assessed by a magnet tracking system. BMC Gastroenterol. 2011;11:145-

17. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. J Biomed Inform. 2019;95:103208.

18. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42(2):377-81.

19. Hedsund C. Magnet tracking allows assessment of regional gastrointestinal transit times in children. Clin Exp Gastroenterol 2013;6:201-8.

20. Velde SV, Notebaert A, Meersschaut V, et al. Colon transit time in healthy children and adolescents. Int J Colorectal Dis. 2013;28(12):1721-4.

21. Arhan P, Devroede G, Jehannin B, et al. Idiopathic disorders of fecal continence in children. Pediatrics. 1983;71(5):774-9.

22. Russo M, Martinelli M, Sciorio E, et al. Stool consistency, but not frequency, correlates with total gastrointestinal transit time in children. J Pediatr. 2013;162(6):1188-92.

23. Wagener S, Shankar KR, Turnock RR, et al. Colonic transit time--what is normal? J Pediatr Surg. 2004;39(2):166-9; discussion -9.

24. Arhan P, Devroede G, Jehannin B, et al. Segmental colonic transit time. Dis Colon Rectum. 1981;24(8):625-9.

25. Gutiérrez C, Marco A, Nogales A, et al Total and segmental colonic transit time and anorectal manometry in children with chronic idiopathic constipation. J Pediatr Gastroenterol Nutr. 2002;35(1):31-8.

26. Shava U, Yachha SK, Srivastava A, et al. Assessment of stool frequency and colonic transit time in Indian children with functional constipation and healthy controls. Indian J Gastroenterol. 2018;37(5):410-5.

27. Southwell BR, Clarke MC, Sutcliffe J, et al. Colonic transit studies: normal values for adults and children with comparison of radiological and scintigraphic methods. Pediatr Surg Int. 2009;25(7):559-72.

28. Locke GR, 3rd, Zinsmeister AR, Fett SL, et al Overlap of gastrointestinal symptom complexes in a US community. Neurogastroenterol Motil. 2005;17(1):29-34.

29. Sharif H, Abrehart N, Hoad CL, et al. Feasibility Study of a New Magnetic Resonance Imaging Mini-capsule Device to Measure Whole Gut Transit Time in Paediatric Constipation. J Pediatr Gastroenterol Nutr. 2020.

30. Fallingborg J, Christensen LA, Ingeman-Nielsen M, et al. Measurement of gastrointestinal pH and regional transit times in normal children. J Pediatr Gastroenterol Nutr. 1990;11(2):211-4.

31. Rodriguez L, Heinz N, Colliard K, et al. Diagnostic and clinical utility of the wireless motility capsule in children: A study in patients with functional gastrointestinal disorders. Neurogastroenterol Motil. 2020:e14032.

32. Nandhra GK, Mark EB, Di Tanna GL, et al. Normative values for region-specific colonic and gastrointestinal transit times in 111 healthy volunteers using the 3D-Transit electromagnet tracking system: Influence of age, gender, and body mass index. Neurogastroenterol Motil. 2020;32(2):e13734-e.

33. Saad RJ. The Wireless Motility Capsule: a One-Stop Shop for the Evaluation of GI Motility Disorders. Current gastroenterology reports. 2016;18(3):14-.

Figure 1: Motilis 3D-Transit system

The 3D-Transit system worn by a healthy child. A belt is worn around the waist, carrying the detector in front and the battery on the side. The capsule measures 21,5 mm x 8,3 mm. A respiratory belt is worn around the chest to record breathing activities. All data are stored on an SD-card located in the detector. B) 3D-Transit overview function: The frequency of contractions (y-axis) plotted against time (x-axis) helps determine pyloric and ileocecal passages by changes in GI contraction frequency. Pyloric passage is recognized as a shift from 3 contractions per minute (cpm) to 9-12 cpm. Ileocecal passage is recognized around the decline from approx. 6 cpm to 3 cpm. C) Pyloric passage in a 3D-Transit recording of a healthy child. The position (x, y, z) and orientation (θ, φ) of the capsule are displayed. The position (X, Y, Z) and orientation (θ, φ) of the capsule are displayed. The 2D-plot (x, y) in the upper left corner displays pyloric passage (yellow dot is equivalent to yellow line) and verified with respect to changes in trajectory and loss of characteristic frequency of gastric motility (three cpm, marked by white arrows).

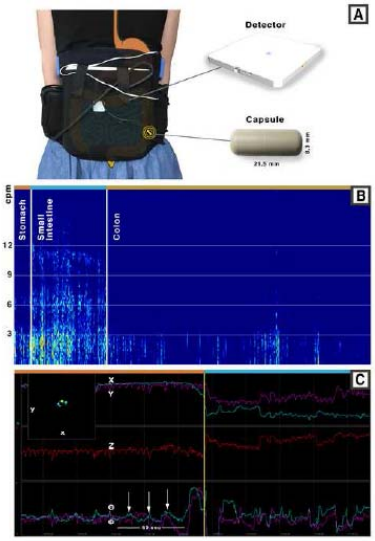

Figure 2: Colonic progression in two healthy children

Two different types of colonic progression. A and B) A total colonic transit time of 28.4 hours characterized by slow, very slow, or no progression for approximately 17 hours in the ascending colon, followed by two long fast antegrade movements (seen as one) covering the transverse, descending, and sigmoid colon. C and D) A total colonic transit time of 26.1 hours characterized by steady progression through all four colonic segments. Arrows mark defecations during the period of colonic transit time.

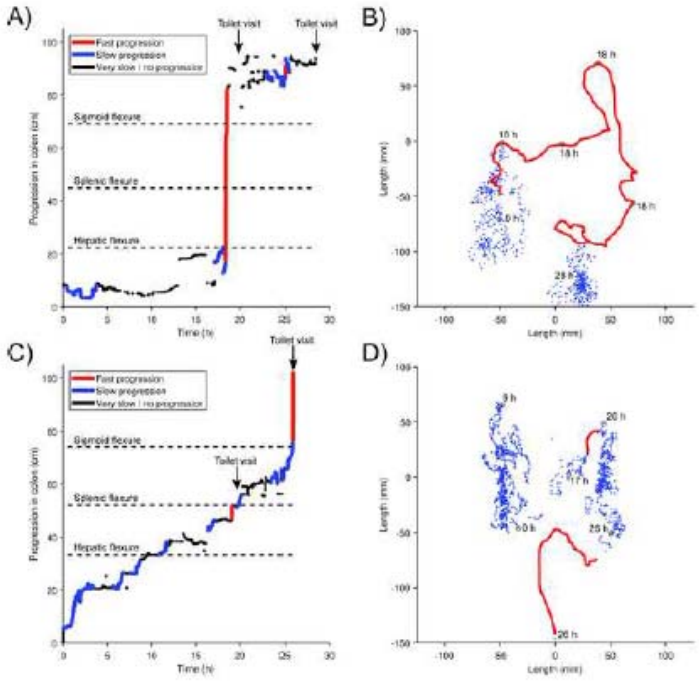

Table 1: Gastrointestinal transit times in healthy children (n = 20)

	Subject number	Gastric emptying time	Small intestinal transit time	Ascending colonic transit time	Transverse colonic transit time	Descending colonic transit time	Rectosigmoid colonic transit time	Total left colonic transit time	Total right colonic transit time	Colonic transit time	Whole gut transit time	Stool frequency*
	1	0.2	15.0	48.1	5.7	1.9	9.7	17.2	48.2	65.4	80.7	2.7
	2	2.0	4.1	0.4	6.8	2.9	13.3	17.9	5.4	23.4	29.4	1.6
	3	2.5	2.9	9.7	10.5	5.8	0.1	9.3	16.7	26.1	31.5	2.3
	4	1.7	7.5	9.4	5.7	22.3	2.5	26.4	13.6	39.9	49.1	2.0
	5	1.9	8.2	18.4	0.0	0.1	9.9	10.0	18.4	28.4	38.6	1.9
	6	1.3	7.1	13.7	9.4	1.3	0.7	8.8	16.3	25.1	33.5	1.4
	7	17.8	4.4	0.3	7.7	0.0	4.6	8.6	4.0	12.6	34.8	2.8
	8	2.6	5.3	1.6	11.6	2.6	7.8	21.6	2.1	23.7	31.7	2.3
	9	2.4	5.1	11.2	0.9	10.1	1.4	12.3	11.3	23.6	31.1	1.5
	10	2.7	1.1	4.3	0.2	1.3	1.0	2.5	4.3	6.8	10.5	4.5
	11	22.1	4.5	8.3	2.8	3.1	16.1	22.0	8.3	30.4	57.0	0.8
	12	1.2	2.1	3.0	1.6	18.6	3.4	22.5	4.1	26.6	30.0	0.8
	13	3.8	4.6	2.7	2.4	7.4	7.4	14.8	5.1	19.9	28.3	1.7
	14	1.4	5.4	10.3	5.7	0.1	10.8	16.0	10.9	26.9	33.8	1.4
	15	1.9	6.7	12.0	2.0	0.1	8.7	8.8	14.0	22.8	31.4	2.3
	16	0.6	3.8	31.9	5.6	5.4	31.6	39.2	35.3	74.5	78.8	1.2
	17	0.1	2.3	29.3	3.5	11.7	0.9	14.8	30.6	45.5	47.8	3.0
	18	1.7	10.9	8.7	5.7	0.0	19.8	22.0	12.2	34.3	46.9	1.0
	19	0.7	4.9	13.4	0.5	0.0	7.5	7.5	13.8	21.3	26.9	1.8
	20	2.0	4.0	13.8	2.1	1.2	25.0	16.5	9.3	47.2	53.2	1.4
All (n=20)	Median	1.9	4.9	10.0	4.6	2.3	7.7	15.4	11.8	26.4	33.6	1.7
	Range	*0.1–22.1*	*1.1–15.1*	*0.3–48.1*	*0.0–11.6*	*0.0–22.3*	*0.1–31.6*	*2.5–39.2*	*48*	*6.8–74.5*	*10.7–80.5*	*0.8–4.5*
	5th / 95th percentile	*0.1 / 19.9*	*1.6 / 13.0*	*0.35 / 40.0*	*0.1 / 11.1*	*0.0 / 20.5*	*0.4 / 28.3*	*5.0 / 32.8*	*3.1 / 42.0*	*9.7 / 70.0*	*18.8 / 80.0*	*0.8 / 3.8*
Boys (n=10)	Median	1.5	4.7	10	3.2	6.7	3.0	14.8	12.5	26.4	32.5	1.6
	Range	*0.1–22.1*	*2.2–7.5*	*2.7–29.3*	*0.1–10.1*	*0–22.3*	*0.1–16.1*	*7.5–26.4*	*4.1–30.6*	*19.9–45.5*	*26.9–57.0*	*0.8–3.0*
Girls (n=10)	Median	1.9	4.9	10.4	5.7	1.3	9.8	16.9	10.8	26.1	36.7	2.1
	Range	*0.2–17.8*	*1.1–15.1*	*0.3–48.1*	*0–11.6*	*0–5.4*	*1–31.6*	*2.5–39.2*	*2.1–48.2*	*6.8–74.5*	*10.7–80.5*	*1.0–4.5*
	Boys vs. girls	*P* = 0.63	*P* = 0.63	*P* = 1.00	*P* = 0.90	*P* = 0.03	*P* = 0.02	*P* = 0.96	*P* = 0.85	*P* = 0.91	*P* = 0.43	*P* = 0.35

Regional GI transit times and segmental colonic transit times for each child. Median and range are presented for both genders, boys, and girls. The 5th and 95th percentile are presented for the whole gourp. Transit times are presented as *hours*. Two recordings display heavily elongated gastric emptying times. All 20 children ate at the end of the four-hour period.
*Stool frequency is calculated as (total number of stools during capsule residence in the GI tract) / (whole gut transit time in hours) / (24 hours).

Table 2: Colonic movement patterns in healthy children (n = 20)

		Cecum and ascending	Transverse	Descending	Sigmoid and rectum	All colon
Long fast antegrade	N	4	9	12	16	41
	M	0 (0–0)	0 (0–1)	1 (0–1)	1 (0–1)	2 (1–4)
Fast antegrade	N	9	12	8	27	56
	M	0 (0–1)	0 (0–1)	0 (0–1)	1 (1–2)	3 (2–4)
Slow antegrade	N	25	30	19	34	108
	M	1 (0–2)	1 (0.5–3)	1 (0–2)	2 (0–3)	6 (3–7)
Slow retrograde	N	10	3	6	7	26
	M	0 (0–1)	0 (0–0)	0 (0–0)	0 (0–0)	1 (0–2)
Fast retrograde	N	2	0	1	1	4
	M	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)

Distribution of six different colonic movement patterns in regard to capsule movement length, velocity, and direction. N = total number of movements. M = median (interquartile range).