Paediatric constipation and functional non-retentive faecal soiling
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Chapter 4

New insight in rectal function in paediatric defecation disorders: disturbed rectal compliance is an essential mechanism in paediatric constipation

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Submitted
Abstract
Background
The contribution of impaired rectal sensitivity in the pathophysiology of paediatric constipation (PC) and functional non-retentive faecal soiling (FNRFS) has been previously investigated using volume-controlled distension protocols. However, tension/pressure is the main determinant of visceral perception.

Aim
To evaluate rectal sensitivity in children with PC and FNRFS using pressure-controlled distension.

Methods
Thresholds for rectal sensitivity (first sensation, urge to defecate and pain), and rectal compliance were determined using a pressure-controlled distension protocol (Barostat).

Results
69 patients with PC (50 M, mean age 10.9 ± 2.2 years) and 19 children with FNRFS (15 M, mean age 10.0 ± 1.9 yrs) were studied and compared with 22 HV's (11 M, mean age 12.7 ± 2.6 years). Sensitivity thresholds were not significantly different between the groups. Rectal compliance was disturbed (increased) in 58% of PC children (P<0.0001 vs., HV's). Rectal compliance in FNRFS patients did not differ from HV's. Rectal faecal impaction at intake was associated with an abnormal compliance in 60% of the PC children (NS vs. 40% of PC children with normal compliance). PC children with an abnormal rectal function required significantly larger rectal volumes necessary to induce an intra-rectal pressure generating the urge to defecate.

Conclusions
Increased compliance but not impaired rectal sensitivity is the most prominent feature in patients with PC. Due to the higher compliance these children require larger stool volumes to reach the intra-rectal pressure threshold triggering the sensation of urge to defecate. Children with FNRFS have a normal rectal function.
Introduction

Constipation and functional non-retentive faecal soiling (FNRFS) are common problems in paediatrics, accounting for respectively 3% and 1-2% of consultations in an average paediatric practice and as much as 25% in a paediatric gastroenterology clinic (1). Paediatric constipation (PC) is diagnosed when at least two of the following four criteria are present: defecation frequency < 3 per week, two or more encopresis episodes per week, production of large amounts of stool every 7-30 days and a palpable abdominal or rectal mass (2). In contrast, FNRFS is defined as defecation into places and at times inappropriate to the social context, in the absence of structural or inflammatory disease and in the absence of faecal retention occurring in a child older than 4 years (3).

In the defecation process, the rectum provides a reservoir, gives rise to the sensation to defecate when filled with faeces, and contracts during defecation. To date, few studies have evaluated rectal function in children with FNRFS (4-6). So far, no abnormalities have been reported, leading to the hypothesis that this clinical entity mainly results from psychological disturbances (3). In contrast, several studies have reported abnormal rectal sensitivity in a substantial proportion (27%-78%) of children with PC (7,8). In these studies, sensitivity was tested by distension of the rectum with increasing volumes (i.e. anorectal manometry). To date, it is however becoming increasingly clear that pressure/tension, and not volume mainly determines visceral perception (9-11). It is also clear that the intra-luminal pressure and the visceral sensation induced by volume controlled distension strongly depend on the compliance of the distended organ. Larger volumes will be required in an organ with a large compliance to induce a similar sensation (pressure/tension), compared to an organ with a much smaller compliance.

These considerations suggest that the previous studies in children with PC/FNRFS using volume controlled distension protocols may have overestimated the role of impaired rectal sensitivity. Therefore, in order to get a better understanding of the true rectal sensitivity and to eliminate the influence of rectal compliance, we designed the present study evaluating rectal function using a pressure controlled distension protocol applied by a barostat in children with PC and FNRFS.
Materials and methods

Subjects

Between August 1996 and November 2003, a group of otherwise healthy children, who were referred to our paediatric gastrointestinal motility lab with complaints of paediatric constipation (PC) or functional non-retentive faecal soiling (FNRFS), were included in this study. All children were at least 5 years of age and thus able to understand the rectal barostat procedure. The study encompassed 88 patients: 69 PC children and 19 patients with FNRFS. These data were compared with data from 22 healthy volunteers (HV's) with no gastrointestinal complaints.

Patients with paediatric constipation were included in the study when they fulfilled at least 2 out 4 following criteria: 1) stool frequency < 3/week, > 1 encopresis episodes / week, periodic passage of large amounts of stool once every 7-30 days, or a palpable abdominal or rectal mass. Functional non-retentive faecal soiling was defined as: > 1 encopresis episode / week, without any other criteria of paediatric constipation as mentioned above. In this study we used the “classic” criteria, because the Rome criteria were not available at the start of this study (2,12). PC children were included when conventional therapy (high fibre diet, high fluid intake, toilet training, oral and /or rectal laxatives) with or without biofeedback training had been unsuccessful. FNRFS patients were included in the study after failure of a strict toilet training regimen and / or biofeedback training. Children with organic causes for defecation disorders / faecal incontinence, including Hirschsprung’s disease, muscle disorders, patients with prior recto-anal surgery, spina bifida (occulta), mental retardation or hypothyroidism were excluded from the study. A faecal scybalus at intake was defined as faecal retention characterized by the accumulation of a large, hard faecal mass in the rectum.

Procedure and equipment

A rectal polyethylene balloon with infinite compliance and a maximum volume of 510 ml was connected to a computer-driven barostat device (Synectics Visceral Stimulator; Synectics, Netherlands), used for controlled inflation. The balloon was fixed on a silicone catheter with an outside diameter of 4 mm and an inside diameter of 3 mm, allowing a flow of air of 38 ml/sec. Before and after each study, the balloon was checked for leakage.
Experimental protocol
Pain medication and all medication known to affect the gastrointestinal motility were discontinued 48 hours before the barostat procedure. One week before the study, the parents and the child were invited to the motility unit to be intensively informed about the equipment and the barostat procedure. Only PC patients received bowel preparation consisting of at least three enemas on three consecutive evenings before the day of the study (Klyx: sodium-dioctylsulfosuccinate / sorbitol; 120 ml). If on rectal examination faeces were present in the rectum, subjects were asked to defecate. Emptiness of the rectum was checked once more by rectal digital examination. The subjects were placed in the left lateral position. The lubricated balloon was introduced into the rectum without the use of endoscopy.

The balloon was unfolded by a stepwise increase (30 ml per step) until a maximum volume of 150 ml. With the balloon still inflated the catheter was pulled back against the pelvic floor. After deflation and a 15 minute period of equilibration, the minimal distension pressure (MDP) was determined by stepwise increasing the intra-balloon pressure (1 mm Hg steps for 1 minute). MDP was defined as the pressure resulting in an intra-balloon volume of at least 30 ml and at which the influence of breathing on the volume could be identified. Determination of MDP was followed by a rectal adaptation period of 15 minutes.

Rectal sensitivity to distension was evaluated using an intermittent distension procedure with steps of 3 mmHg lasting 1 minute and intervals of 1 minute. At every pressure step the child was asked to score sensation immediately and after 30 seconds. An ordinal scale from 0-5 was used (13): 0=no sensation, 1=first sensation, 2=urge to defecate, 3=moderate urge to defecate, 4=severe urge to defecate, 5=pain. In case of pain, the balloon was immediately deflated. The study protocol was approved by the medical ethical committee of the Academic Medical Centre. All subjects and/or parents gave informed consent.

Analysis
**Rectal sensitivity**
Thresholds for first sensation, urge to defecate and pain were determined from the intermittent distension protocol and expressed as pressure above MDP. If individuals did not reach a threshold during barostat (for example no pain), they were given the highest possible threshold (i.e. MDP + 39 mmHg).
Rectal compliance

The compliance, a measure of rectal distensibility and a resultant of the elastic properties of the rectal wall (14), was calculated using a non-linear mixed-effect model for fitting the pressure volume curves of each individual (15,16). The pressure volume curves were constructed using the mean volume of the last 15 seconds (when equilibration of the volume was reached) at each of the consecutive pressure steps.

In a first analysis all curves were fitted individually to a 4 parameter logistic curve, using non-linear regression analysis. This provided the parameters C (compliance: maximum slope in the Volume-Pressure curve), V0 (volume at time point zero), and Vm (maximum volume) for each individual as well as their standard errors. The fourth parameter was introduced to improve the fit of the logistic curves. It consisted of a hypothetical starting volume at negative infinite pressure, common to all patients. The value of this parameter itself is of no importance and therefore not reported. The SD of the within patient measurement error was assumed to be equal for all individuals.

In a second analysis the individual parameters C, V0 and Vm were assumed to be derived from a 3-dimensional normal distribution, leading to a non-linear mixed effect regression analysis. No assumptions were made about the correlations between the three parameters. Group means and SD's for C, V0 and Vm were derived from this analysis, which corrected these values for within-patient variability.

Statistical analysis

Baseline patient data are expressed as mean (± SD). Sensation thresholds are described as median value above MDP together with their 5th and 95th percentile. If an individual had a sensitivity threshold above the 95th percentile (i.e. 'cut-off' above the median value of the HV's), he was considered to be above the upper limit of normal. Because of the distribution of data, non-parametric tests (Kruskal-Wallis / Mann Whitney) were used for comparing sensation thresholds and compliance. The Chi-square test was used to compare the number of patients in each group, who reached the threshold for sensation of urge, pain, and compliance. The Pearson's correlation coefficient was used to calculate correlation coefficients. Differences were considered statistical significant when the p-value was less than 0.05.
**Results**

**Subject characteristics**

Sixty nine PC patients (50 boys, mean age 10.9 ± 2.2 years; range 7 – 15 years) and 19 children with FNRFS (15 boys, mean age 10.0 ± 1.9 years; range 6 – 13 years) were studied and compared to 22 HV’s (11 boys; mean age 12.7 ± 2.6 years; range 7 – 16 years). Clinical characteristics are shown in table 1. Age at time of study was significantly different between patients and HV’s (PC vs. HV’s and FNRFS vs. HV’s both p=0.002, Kruskal-Wallis). The duration of symptoms before the barostat procedure in the PC and FNRFS group was 6.7 ± 2.9 years and 6.0 ± 2.0 years, respectively. Constipated children had been treated for 36.0 ± 37.0 months prior to intake while FNRFS patients were treated for 18.8 ± 25.9 months.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Subject characteristics at time of barostat</th>
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</thead>
<tbody>
<tr>
<td>PC</td>
<td>N = 69</td>
</tr>
<tr>
<td>HV’s</td>
<td>N = 22</td>
</tr>
<tr>
<td>FNRFS</td>
<td>N = 19</td>
</tr>
<tr>
<td>Number of boys (%)</td>
<td>50 (72%)</td>
</tr>
<tr>
<td>Age (in years)</td>
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</tr>
<tr>
<td>Defecation frequency</td>
<td>2.3 ± 2.4 (0-12.5)</td>
</tr>
<tr>
<td>Encopresis frequency</td>
<td>11.0 ± 12.7 (0-70)</td>
</tr>
<tr>
<td>% of subjects with large stool every 7-30 days</td>
<td>72</td>
</tr>
<tr>
<td>% of subjects with scybalus</td>
<td>44</td>
</tr>
</tbody>
</table>

Results are shown as mean (± SD) unless otherwise specified

**Rectal sensitivity to distension**

**Minimal Distension Pressure (MDP)**

MDP was 5 ± 2 mmHg in PC children, 6 ± 2 mmHg in children with FNRFS, and 4 ± 2 mmHg in HV’s (P=0.001, Kruskal-Wallis). The mean volume in the barostat balloon at MDP was 39 ± 27 ml (PC), 46 ± 27 ml in patients with FNRFS, and 31 ± 13 ml in the HV’s (NS).
**First sensation**

The threshold for first sensation was 3 (0-6) mmHg above MDP in HV's (median (5th-95th percentile)), with 6 mmHg above MDP as the upper limit of normal range. No significant difference in threshold for first sensation was found between the three groups (PC: 3 (0-8) mmHg, FNRFS: 3 (0-9) mmHg, and HV’s: 3 (0-6) mmHg above MDP, respectively). In the PC and FNRFS group, 13 (19%) and 3 patients (16%) had a threshold for first sensation above the upper limit, respectively. This was not significantly different compared to HV’s (figure 1a).

**Urge to defecate**

The threshold for urge to defecate was 6 (0-19) mmHg above MDP in HV’s, with 19 mmHg (95th percentile) above MDP as the upper limit of normal range. The 3 groups were not significantly different with respect to urge to defecate (PC: 6 (0-39) mmHg, FNRFS: 6 (0-30) mmHg, and HV’s: 6 (0-19) mmHg above MDP). 7% of PC children and 5% of FNRFS patients (both NS vs. HV’s) had an urge to defecate above the upper limit compared to HV’s. Only 4 PC children reported no urge to defecate (figure 1b).

**Pain**

The threshold for pain was 20 (9-39) mmHg above MDP in HV’s, with 39 mmHg (95th percentile) above MDP as the upper limit of normal range. The threshold for pain was not significantly different between the 3 groups (PC: 23 (10-39) mmHg, FNRFS: 21 (12-39) mmHg, and HV’s: 20 mmHg (9-39) above MDP). Nineteen PC patients (28%), and 3 FNRFS children (16%) reported no pain at all (Both NS vs. HV’s) (figure 1c). There were no significant clinical differences such as defecation frequency and number of encopresis episodes between patients (FNRFS and PC) with a normal and an impaired visceral sensation (urge to defecate as well as pain).
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Thresholds for first sensation

Figure 1a: Thresholds for first sensation.

Thresholds for urge

Figure 1b: Thresholds for urge to defecate.

Thresholds for pain

Figure 1c: Thresholds for pain.
NOTE: None of the individuals above the upper limit of normal reached the threshold for pain.
Rectal compliance

The rectal compliance was 16 (12-20) ml / mmHg in HV’s (median (5th-95th percentile)), with 20 ml / mmHg (95th percentile) as the upper limit of normal range. The rectal compliance in PC children was 22 (11-45) ml / mm Hg and was significantly higher compared to HV’s (16 (12-20) ml / mmHg) and to FNRFS patients (14 (9-24) ml / mm Hg) (P<0.0001, Mann Whitney; PC vs. HV’s and vs. FNRFS). Children with FNRFS did not differ from HV’s (figure 2a). Mean compliance curves in all three groups are shown in figure 2b.
Interaction between compliance and rectal sensitivity (urge to defecate) in constipated patients

Disturbed rectal sensitivity is believed to result in faecal stasis (17) resulting in increased compliance. To evaluate this possible interaction, we evaluated whether increased compliance occurred more often in subjects with impaired sensation defined as an abnormal threshold for urge to defecate (figure 3).

Rectal compliance was disturbed in 40 PC patients. In 90% of these patients a normal rectal sensitivity was found, whereas 4 PC patients (10%) showed an abnormal sensitivity.

At intake, 44% of PC patients had faecal stasis as evidenced by rectal digital examination. In these children abnormal rectal compliance was not different from those without faecal stasis (60% vs. 40%). These findings argue against the assumptions that abnormal rectal compliance is secondary to faecal stasis. In 28 constipated children, both compliance and sensation for urge were normal (41%).

As shown in figure 3, seven PC patients reported urge at MDP. The mean age of these patients was $9.9 \pm 1.9$ years. Two of these patients reported pain at 12 mmHg above MDP, two at 15 mmHg and one at 18 mmHg above MDP, and two patients did not report pain at all.
Rectal volume at urge to defecate
In order to be able to compare our current findings with previous studies using volume-controlled rectal distensions, we determined the corresponding balloon volume at the pressure threshold for urge to defecate. We hypothesized that a disturbed compliance as well as abnormal rectal (pressure) sensitivity would result in an increased balloon volume.

The mean volume (± SD) measured during barostat at the threshold for first sensation, sensation of urge and sensation of pain/discomfort in HV’s was 39 ± 22 ml, 82 ± 38 ml and 197 ± 89 ml, respectively. A correlation was observed between age and visceral sensation (urge) measured as volume (P=0.02) (Pearson correlation coefficient: 0.48). No correlation was observed between age and rectal compliance in HV’s. Rectal compliance did not differ between male and female HV’s.

As shown in figure 4, significant higher intra balloon volumes (mean ± SD) were observed at the threshold for urge to defecate in PC patients with an abnormal compliance plus a disturbed urge (240 ml ± 28 ml), and in those with an abnormal compliance only (169 ± 83) compared to both HV’s (82 ± 38 ml) and compared to PC children with a normal rectal function (96 ± 59 ml) (P<0.001). PC patients with a normal rectal function did not differ from HV’s with respect to intra balloon volumes at the threshold for urge to defecate. Only one patient had an abnormal urge to defecate in the presence of a normal compliance (NS vs. no abnormalities/HV’s).

FNRFS patients needed a balloon volume of 100 ± 50 ml to induce urge (P=0.03 vs. PC, NS vs. HV’s) to defecate whereas in HV’s a volume of 82 ± 38 ml in the barostat balloon was required (P<0.01 vs. PC).

![Figure 4: Volume at urge to defecate in all subjects.](image_url)

HV’s: Healthy volunteers, FNRFS: Functional non-retentive faecal soiling, PC-N: PC patients with no abnormalities during barostat, C&S: PC patients with a disturbed compliance AND sensitivity, C: PC patients with disturbed compliance only, U: PC patient with a disturbed sensitivity only.

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Discussion
In this study assessment of visceral perception using pressure controlled distensions failed to reveal decreased rectal sensitivity as main pathophysiological mechanism in children with severe constipation. Instead, increased compliance occurring in 58% of these patients was the most prominent feature, explaining the higher volume thresholds (sensitivity) described in previous studies. Due to the higher compliance these children require larger stool volumes to reach the intra-rectal pressure threshold triggering the sensation of urge to defecate. FNRFS patients have a normal rectal function, underscoring the earlier clinical and manometric findings that FNRFS constitutes a different clinical entity.

Perception of the urge to defecate plays an important role in the process of normal defecation. Consequently, impaired rectal sensitivity is considered an important mechanism contributing to defecation disorders in childhood, like PC and FNRFS. As the sensation of urge results from rectal filling, experimental protocols distending the rectum have been repeatedly used in both children and adults to evaluate sensitivity. In contrast to previous studies, we assessed rectal sensitivity using a pressure-controlled distension protocol. This choice was based on the knowledge that visceral sensation is determined by pressure / tension receptors (9-11). In this study, we showed that the main mechanism involved in PC is an increased rectal compliance, with 58% of patients showing a rectal compliance above the upper limit of normal. Most importantly, only in 10% of patients with an abnormal rectal compliance rectal sensitivity was impaired. Furthermore, only one PC child had an isolated abnormal rectal sensitivity.

These findings strongly contrast with earlier studies reporting impaired rectal sensitivity in up to 70% of PC patients (7,18). It should be emphasized that in these studies rectal sensitivity was assessed using volume-controlled distension. Especially in the presence of an increased rectal compliance, this method will reveal larger volumes at the pressure threshold of perception of urge to defecate, thereby leading to an overestimation of the prevalence of impaired rectal sensitivity. This reasoning was confirmed when we determined the volume in the barostat balloon at the pressure threshold of urge to defecate. Although higher volumes were measured in PC children with an abnormal compliance, the pressure controlled perception was not disturbed in the majority of these patients. Based on these findings, we suggest that the increased volume thresholds reported earlier are
most likely secondary to an abnormal, increased rectal compliance, and should not be interpreted as impaired rectal sensitivity.

How should our findings be translated to the clinical picture of PC? As shown in figure 4, both decreased rectal sensitivity and increased rectal compliance will result in higher barostat balloon volumes at the threshold of urge to defecate. Clinically this means that these children in contrast to those with a normal rectal function, will require larger stool volume filling the rectum before the sensation of urge to defecate is triggered, contributing to the symptomatology in PC with large intervals between defecation.

Clearly, other mechanism must be involved explaining the reduced defecation frequency in PC children with a normal rectal function. Indeed, similar to the observation in adults (19,20), 41% of our PC group had both a normal rectal compliance and sensitivity to rectal distension, but yet fulfilled the criteria of PC. Most likely other mechanisms, such as impaired colonic motility or psychological factors (20) are involved in the pathophysiology of paediatric constipation.

It is often assumed that abnormal rectal compliance is the result of long-lasting accumulation of faeces. In the current sample however, patients with a normal and an abnormal compliance did not differ significantly with respect to the presence of faecal impaction, making this reasoning less likely. Alternatively, abnormal compliance of the rectum might be the primary cause of faecal impaction. One might assume that impaired excitatory input to the rectum may lead to a decrease of rectal tone and an associated increase in rectal compliance leading to accumulation of faeces (19). Whether the observed change in rectal compliance is primarily or secondary can not be determined from the present data, but can only be investigated in longitudinal studies.

In contrast to PC children, previous studies in children with FNRFS, failed to reveal abnormalities during anorectal manometry (4-6). Therefore, these children were believed to suffer from psychological disturbances only (3). Earlier studies using the child behaviour checklist showed that in FNRFS patients behaviour was abnormal in 35% (4). An association was found between successful treatment and improvement of abnormal behaviour scores (4). This supports the idea that encopresis has an aetiological role in the occurrence and maintenance of behavioural problems in children with FNRFS. In the current study, only 5% of children with FNRFS showed disturbed urge to defecate and 16% a disturbed threshold for pain
(both NS vs. HV's). Also in contrast to PC children, the majority of FNRFS patients demonstrated a normal compliance. The fact that FNRFS patients, as opposed to constipated children, have a normal rectal compliance, have a normal defecation frequency, no faecal impaction on physical examination (3), and a normal colonic transit time (21) further underscores that FNRFS is a different clinical entity compared to constipation. More research is warranted to further clarify the pathophysiology of the encopresis in FNRFS patients.

In conclusion, increased rectal compliance and not decreased rectal sensitivity is the major pathophysiological mechanism in children with chronic constipation. Due to the higher compliance these children require larger stool volumes to reach the intra-rectal pressure threshold triggering the sensation of urge to defecate. Longitudinal studies evaluating rectal function have to establish whether increased rectal compliance is a primary or secondary phenomenon. In accordance with previous studies children with functional non-retentive faecal soiling have no obvious abnormalities during rectal function testing emphasising that FNRFS is a separate clinical entity.
References


