Chapter 15

TRANSCUTANEOUS ELECTRICAL STIMULATION OVER THE BELLY IN SLOW-TRANSIT CONSTIPATION

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INTRODUCTION

Slow-transit constipation (STC) is a condition where there is poor motility in the whole colon. STC is generally resistant to current treatments. Previous chapters have discussed constipation in great detail. For this chapter it is important to emphasise that chronic constipation is a lifelong problem that begins in childhood and continues into adulthood for 1/3 of patients [1-6]. Thirty-six % of adults fail non-surgical therapies (diet, bulking agents, laxative or biofeedback). In the 1990’s, 90% of paediatric chronic constipation was classified as ‘idiopathic’, and assigned to behavioural / psychological causes due to children avoiding painful defecation [6-7]. However, behavioural problems resolve after adequate treatment of the constipation, suggesting they are secondary to constipation [3]. Within the gastroenterology field, chronic constipation with no known organic cause is now described as a ‘functional disorder’ meaning that function is affected.

SLOW-TRANSIT CONSTIPATION:
COLONIC TRANSIT STUDIES

There are two methods to determine where the site of hold-up occurs within the bowel: 1) plastic markers with x-rays (Sitz marker studies) provide information on the speed of transit through the colon and if there is holdup in the colon or rectum: 2) radioisotope transit studies (scintigraphic studies) have the added advantage with images acquired at different times allowing measurements of gastric emptying, small bowel transit, regional colonic transit and transit through the rectum to be quantified [8]. Scintigraphic transit studies have been available at specialist centres for the last 10-20 years and methods are developing to a point where they will be able to be used by radiologists at many major hospitals, though with modified protocols. Normal rates of transit are well-defined for adults and children. Based on colonic transit time, persistent constipation has been divided into three categories: 1) anorectal retention (outlet obstruction, dyssynergic defecation, functional faecal retention), 2) slow colonic transit (slow transit constipation, STC) and 3) normal transit [8-9]. Approximately 70% of children with chronic treatment-resistant constipation have anorectal retention and 20% have slow colonic transit [3,7,10]. Anorectal retention can also occur with STC. Very long transit studies may be needed to see the combined conditions. In our studies, we see them only in a small number of children with STC as our transit studies only last 48 hours. Studies in adults are performed for 72 or 96 hours and reveal STC with AR. It is generally thought that slowing in the proximal colon is secondary to the retention in the anorectum, due to inhibitory ascending neuronal reflexes. But there is no evidence to determine which is the primary defect.

We have done radioisotope colonic transit studies since 1997 [9,11-12]. We now have 955 studies on 667 children with chronic constipation with the studies collected into one database. Children with a palpable faecaloma were easily defined as having stool retention in the anorectum and were rarely sent for transit studies. The test was used for children with chronic constipation without a faecaloma, where we needed to determine where the defect in motility was occurring. In the 667 children (309 female, 2-23 yrs, mean 8.4 yrs), 133 (20%) had normal colonic transit, 344 (52%) slow colonic transit (STC, Figure 1) and 190 (28%)
had rapid proximal colonic transit with anorectal retention in ½ of this group. Based on our experience with this technique, in our research group, we identify normal transit rates by the amount of radioactivity in each region using the criteria listed in Table 1. We have recently described the details of the scintigraphy method (in children) for radiologists giving specific details for measuring regional and intestinal transit [13].

Figure 1. Diagnosis of Slow-transit Constipation (STC) by radionuclear transit study. Children were given a milk drink containing the radioisotope and images were taken using a gamma camera (A). The radioactivity is tracked as it moves through the stomach, small intestine and colon (B). Images are taken at 6hr, 24 hr, 30 hr and 48 hr after the milk drink (C). In normal transit, > 40% of the radioactivity is excreted by 30- 48 hours. In this example of STC, radioactivity is moving slowly through the ascending and transverse colon and only reaches the descending colon at 48 hrs after the milk drink. Criteria used to define normal transit are given in table 1.

### Table 1. Criteria for Normal gastric emptying, small bowel transit, colonic transit and anorectal transit

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal Values</th>
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<tbody>
<tr>
<td>Gastric emptying – Images</td>
<td>t½ (half-emptying time) ≤ 50 mins</td>
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<tr>
<td>at 0, 30, 60 and 120 mins</td>
<td>Gastric emptying at 2 hr ≤ 15% of counts still in the stomach at 2hrs</td>
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<tr>
<td>Small bowel transit</td>
<td>≤ 25% of radioisotope retained in small bowel at 6 hr</td>
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<tr>
<td>Colonic transit</td>
<td>24 hr: &lt; 40% of radioisotope retained in trans colon</td>
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<td></td>
<td>48 hr: &lt; 30% of radioisotope retained in trans colon</td>
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<tr>
<td></td>
<td>Geometric centre (GC): &gt; 3.0 at 24 hr and/or &lt; 4.2 at 48 hr</td>
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<tr>
<td>Anorectal transit</td>
<td>48hr: &gt; 40% of radioisotope excreted</td>
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Criteria used to assess scintigraphy (radioisotope transit and gamma camera images) at Royal Children’s Hospital, Melbourne, Australia. For geometric centre (GC), 6 regions of interest are defined: 1 small bowel, 2 ascending colon, 3 transverse colon, 4 descending colon, 5 recto-sigmoid colon, 6 excreted. Percentage is the fraction of the total radioactivity given.

Two hundred and eighty-eight children have had repeat studies. Some studies have been performed after medical treatment to determine if there has been any change. In patients who have no change in symptoms (treatment-resistant), transit studies performed 2 years apart gave similar results [14]. Recently we have identified fast transit in the small intestine associated with constipation. This condition may be associated with food allergy or
intolerance. We have also shown that many children with STC but not AR have an elongated colon (also called redundant colon) [15].

**STC CHILDREN HAVE LOW NUMBERS OF PROPAGATING CONTRACTIONS IN THE COLON**

Figure 2. Multichannel colonic manometry showed low activity in STC prior to transcutaneous electrical stimulation (TES). A. Propagating contractions are low in children with STC compared to normal healthy young adults. Contractions measured using 8 or 16 channel water perfused manometry catheters. Measurements for 24 hours. B. TES increased the number of propagating contractions into the normal range. Pre was measured just before the first stimulation session. Post was measured 2 months after TES ceased. TES for 1 month, 20 min /day, 3 days /wk. Ant=antegrade, Ret= retrograde, HAPS= high amplitude propagating sequences.

Mutli-channel water-perfused catheters have been used to measure propagating contractions within the colon and analyse strength, direction and distance propagated [16-17]. Most of these studies have been done in adults. Normally, at night, there is a decrease in total activity, while during the day there is an increase in activity after a meal. Waves of propagation go upstream and downstream in the colon, allowing intensive mixing of contents [18,19]. Contraction of the proximal colon occur just prior to defecation. While it was originally thought that high amplitude propagating contractions (HAPS) were required for propulsion, studies in rabbits show that propulsion occurs with low amplitude propagating contractions [20]. In 24-hour studies of 18 children with STC, we found a significant impairment in antegrade propagating motor activity (29 +/- 4 per 24 h in STC compared to 53 +/- 4 per 24 h in adults and 70 +/- 14 per 24 h in non-STC children) and failure to respond to normal physiological stimuli (waking and meals). HAPS were reduced but not significantly (Figure 2A). We also found high amplitude retrograde propagating sequences in STC and non-STC pediatric groups [21,22]. At Nationwide Childrens Hospital in Ohio, STC is diagnosed as the absence of HAPS in 4 hour studies [23]. The average number of HAPS in 24 hours is 10 in healthy controls. Using new fibre optic catheters with sensors every 1cm, Dinning et al have shown that propagating contractions are missing in the middle of the transverse colon in adults with STC [24].
APPENDIX STOMA

Figure 3. STC children were managed with appendix stomas and antegrade continence enemas (ACE) prior to the development of transcutaneous electrical stimulation (TES). A. Appendix stoma just after formation. The appendix is brought out through the skin, the tip is cut off and the appendix sewn to the skin. The appendix forms a conduit to the caecum that is lined with mucosa. A Chait caecostomy button is placed into the stoma. The Chait catheter has a straight section and then a spiral section that locates in the caecum. The button has a trapdoor to close and prevent seepage. Children connect a catheter to the outside of the button and deliver a laxative solution directly into the caecum to produce an antegrade enema, with stool released through the anus. We have used this as a management procedure for patients who had not responded to other treatments and were candidates for colectomy (removing the colon). B. Number of appendix stomas placed each year at our hospital. Since commencing TES, many patients have had success and the number having appendix stomas has reduced. Patients who fail TES still have the option of an appendix stoma.

A number of groups use appendix or caecal stomas as a management option and have reported good success with children [23,25-33]. We bring the tip of the appendix out through the skin, cut off the tip and sew the appendix to the skin to create a conduit to the caecum (Figure 3A). We then place a ‘Chait’ caecostomy button into the stoma [34-37]. Children introduce a solution into the caecum to ‘washout’ the colon. This antegrade enema stimulates the proximal colon and stool are passed through the anus into the toilet. Appendix stomas have less problems than caecostomies, as the appendix is lined with mucosa and there is no leak into the body wall and the Chait button reduces stomal constriction and erosion. We have found that some children no longer need to use the appendix stoma after a few years [35]. It may be that the bowel starts working properly if the stool is continually removed and the bowel is no longer stretched.

NERVES COORDINATE INTESTINAL MOTILITY
(SEE CHAPTER 18)

The intestine contains its own nerve cell bodies that form a network (enteric nervous system) and connect to the central nervous system [38-39]. These neurons have cell bodies within the myenteric or submucosal plexuses and send processes into the muscle layers, where they release transmitters. Changes in subgroups of enteric nerve fibres occur in association with motility disorders [3,11.40-43]. The large bowel is connected to the central
nervous system (CNS) via the vagal, splanchnic and pelvic nerves. Each of these carry sympathetic, parasympathetic and sensory nerve fibres [44]. Sympathetic innervation (coming from spinal cord levels T5-L2, via the splanchnic nerve) inhibits motility, while parasympathetic innervation (via the vagus nerve and pelvic nerves derived from sacral segments S2-S4) activates the colon. Pelvic nerves also carry parasympathetic outflow to the rectum and internal anal sphincter and somatic innervation to the striated anal sphincter muscle [44]. All of these nerves also carry sensory fibres to the CNS.

Nerves are voltage activated cells and are affected by electricity. Therefore, electrical stimulation is being used to activate nerves and modify gastrointestinal activity. Since the discovery of electricity, it has been clear, that current applied to the body can make the bowels release their content. While it is clear that electric stimulation with high currents (such as with the electric chair) causes the bowels and bladder to empty, treatment using lower levels of electrical stimulation are usually met with scepticism. Particularly if the effect does not occur at the time of stimulation. One of the earliest reports that electrotherapy could induce laxative effects was described in 1749 by Jean Jallabert, a Genevan Professor of experimental philosophy and mathematics [45]. Jallabert attempted to cure a patient of muscle paralysis using “electrification”, where electrical energy was provided by a Leyden jar. (Leyden Jars were used before the development of batteries to store electric charge. A circuit was created by placing the hand on the outside of the jar.) On a cold day, Jallabert used warm water in the Leyden jar instead of cold water, as cold water was uncomfortable for his patient. His patient noted that the electrification was stronger, painful and caused severe diarrhoea [45-46]. The French clergyman Jean-Antoine Nollet tested electrification for these purgative effects including testing it on himself in 1749 over a period of 4 days [47]. Nollet’s diarrhoea episodes did not begin immediately and at the time, his demonstration was ridiculed [45]. Nollet acknowledged that the experiment he conducted on himself may have been affected by some foods that caused him bowel discomfort on the third day of his experiment [47]. It is clear that controversy surrounded the effectiveness of electrification as a purgative agent and Nollet said he doubted the testimonies of lower classes, servants and women who he considered were not reliable [47]. It was also reported at the time that electrification often took months or weeks to exert a therapeutic effect [45], and of course it is difficult to prove association when the effects take so long to see.

In the latter half of the 19th century, the famous electrical engineer and inventor Nikola Tesla also demonstrated that electrical stimulation could induce immediate laxative effects. In an incident where the American novelist Mark Twain visited Tesla’s laboratory in New York, Twain experienced a laxative effect after standing on a device (large electrical plate) that provided an alternating current electrical stimulation [48]. In this case, the effects were developed during stimulation and sent Twain rushing for the toilet. The effect was well known by the laboratory staff and the time of onset of the effect was predictable.

Direct electrical stimulation has been harnessed to stimulate anal sphincter contraction using direct stimulation of the sacral nerves [49]. With this stimulation, the effects are seen at the time of stimulation. Recently SNS is being used to treat constipation (See Chapter 13). Direct stimulation of sacral nerves initiates colonic contraction and movement of faeces into the anal canal. Reflex pelvic floor relaxation follows, with evacuation of the rectum [50]. S3 stimulation initiates high-pressure colorectal motor activity that appears peristaltic and is enhanced by repetitive stimuli. S4 stimulation increases colonic and rectal tone and produces sustained contractions of the external anal sphincter [44]. In the last 5 years, neural
stimulation using electrodes implanted over the sacral outflow has been trialled in women with idiopathic constipation [51-52], as a diagnostic test [53], and as a treatment for patients with severe faecal incontinence due to deficits of the external anal sphincter [54-57]. Some patients experienced pain or electrode migration that prompted electrode removal [56] and raised concerns for use in children. Recently, the method has been tested in children with success [49]. The treatment is expensive ($18,000-$30,000/patient).

**TRANSCUTANEOUS ELECTRICAL STIMULATION (TES)**

Use of transcutaneous stimulation to treat children with STC was recently reviewed briefly [58]. Physiotherapists have used TES using an interferential current (Figure 4) for over 20 years to treat bladder over-activity and urinary incontinence, and to strengthen the pelvic floor [59-63].

![Figure 4. Interferential stimulation - a special type of of transcutaneous electrical stimulation (TES). A. For this current, 4 electrodes are used. Leads are connected so the currents cross within the abdomen. B. The two currents are out-of-phase (for example 4000 Hz and 4100 Hz) and interfere with each other where they meet to produce an ‘interference current’. The amplitudes of the currents are summed producing a sinusoidal beating current. Currents of 50Hz or less activate striated muscle producing abdominal muscle contraction, and pain fibres producing pain. Currents of >100 Hz can penetrate deeper without causing striated muscle contraction or pain. We used a current that switched from 80 Hz to 160 Hz in steps and back down each minute. Current was applied just at the sensory threshold and is perceived as a pleasant beating tingle. Current was 20-30mAmps. If the currents do not cross, they do not interfere to produce the summed currents. Patients who did not cross the currents did not have any effects, but did have improvement when they did cross the currents.](image)

When used for urinary incontinence, TES has also produced diarrhoea [64-67] suggesting to our experienced continence Physiotherapist Janet Chase that TES could be used to treat constipation. Together with Dr Susie Gibb, a paediatrician specialising in continence, she performed a pilot study on 8 children with chronic treatment-resistant constipation (STC or low levels of substance P-containing nerve fibres in colon circular muscle). TES increased defecation in 5/8 children and stopped soiling in 7/8 [68]. Positive effects lasted >3 months in 3/5 responders [68]. In initial studies, children attended physiotherapy clinics and treatment was performed by physiotherapists who were experienced in electrical stimulation (Table 2).
They used Metron interferential stimulators that plugged into 240 V mains power. Battery-powered interferential stimulators became available in 2008 and we were then able to send patients home to do stimulation themselves. This allowed us to have stimulation done each day. We found that detailed education was required for patients to do the method correctly. It required 6 patients for a naive clinician to learn how to get everything correct in teaching the method and data collection. It was particularly important to make sure the patients connected the leads so that the currents cross to produce the interference current (Figure 5). Four sticky electrodes are placed, 2 on the belly and 2 on the back for the period of stimulation. Stimulation is given with a carrier frequency of 4kHz and beat frequency of 80-160Hz, at 20-30 mAmps. Stimulation is non-invasive, painless and safe. The stimulation is given at the sensory threshold and perceived as a comfortable tingling sensation.

In 2006-2009, we performed a randomised controlled trial (RCT) of TES on 46 children with STC. Children were randomly assigned to receive full or sham stimulation. Stimulation was performed by physiotherapists to control treatment parameters and enabled sham stimulation with specially adjusted machines that looked identical to normal machines, with dials that moved but did not deliver current. Children were given 20 minutes stimulation 3 times a week for a month.

The TES produced small changes in some parameters in patients given active stimulation (Figure 6). There was a significantly increase in the speed of transit [69], decreased soiling, and increased quality of life [70]. Improvements occurred significantly more in the active than in the sham group, but there was no significant difference between the groups. Thirty four children had radionuclear transit studies (NTS) after stimulation (21 M, 8-17 years, mean 11.3 years; symptoms >9 years). In further analysis we found that active stimulation sped up transit in >50% of patients versus only 25% given sham stimulation (p=0.04) [71]. Our method for measuring colonic transit, the radionuclear transit study, also gives us data on gastric emptying and small bowel transit. We found that 17/34 children had concurrent upper gastrointestinal dysmotility (UGD). When we separated the patients with normal upper GI motility and those with UGD, we found that after 2 months TES, the mean transit rate significantly improved in the group of patients with normal upper GI motility (Geometric
Transcutaneous Electrical Stimulation Over the Belly

centre, GC pre-stimulation 3.6 +/- 0.6, GC post stimulation: 5.0 +/- 0.2, p < 0.01) but not in the group with UGD. In the combined group, the change in transit rate was not significant [71].

We also measured intraluminal pressures using 24hr colonic manometry in 7 patients both before and 2-7 months after TES treatment. There was a significant increase in frequency and amplitude of antegrade propagating contractions (Figure 2B) [83].

In the RCT, the primary outcome measure was change in defecation frequency. We expected the children to have <3 defecation/week, however we discovered that many of the children had >3 defecation episodes per week at the start of the study as they were on laxatives for treatment. Only 25% of the children had <3 defecation per week at the start of the trial. After a month of stimulation, defecation frequency only increased in 4/46 children (Figure 6A). In hindsight, defecation frequency is a poor outcome measure for children with STC as they cannot increase the number of defecations if they are already defecating each day. In subsequent studies we have divided the children into two groups: those with >3 and those with <3 defecations/week. For children who started with > 3 bowel action/wk, we need
to measure other parameters (e.g. urge to defecate, size of stool and stool consistency and soiling frequency) as outcome measures.

We performed a long-term follow-up 2-4 years after they had stimulation in the trial [72]. We asked the children if they had improvement after the stimulation and how long they thought it lasted. Two thirds thought they had improvement. In one third of children, improvement lasted 3-6 months, and in one third it lasted more than 2 years. One third had no improvement [72]. Many had stopped or decreased laxative use.

Half (25/46) of the STC patients had no sensory input in the rectum and no urge to defecate. For management, these patients sit on the toilet for a predetermined time for a few sessions each day (called timed-sits). After 2 months' stimulation, in 25 patients who had no urge to defecate before the stimulation, 20 developed the urge to defecate [72]. This suggests that TES activated sensory perception in the rectum. This may give a clue that the mechanism of action of TES is activating sensory endings in the rectum or anus (see below). A number of research studies have identified sensory nerve endings in the rectum [73-79].

Battery-operated machines became available in 2008 making home-based stimulation possible. The advantage of home stimulation is that it can be given every day increasing the dose of stimulation. Eleven children who had been in the RCT, took machines home and administered daily stimulation for 2 months. In this group, defecation frequency was <3/week at the start. In 8/11, defecation frequency increased into the normal range (from 2.5±2.1 to
6.7±4.4/week, mean±SD, p=0.008 paired t test), suggesting that more frequent stimulation is required to increase defecation [80].

Figure 7. TES daily increased defecation and decreased soiling. A. Episodes of defecation/wk. In patients who started with less than 3 defecation/wk, there was a significant increase in defecation after stimulation for one hour per day for 3-6 months. B. Soiling episodes/wk. There was a significant decrease in soiling after stimulation for one hour per day for 3-6 months.

Figure 8. TES developed sensory perception in the rectum and increased the urge to defecate. Data from a single patient showing A. Total number of defecation episodes per week. This child was taking laxatives and had 5 defecation episodes/wk at the start of the study (baseline). Stimulation was given daily for 1 hour for 2 months. After this, defecation increased to 7 episodes/wk. B. The child sat on the toilet at predetermine times each day as part of their management. Initially the number of timed-sits increased, and then decreased to zero. C. Defecation in response to a recognised urge to defecate. This decreased during stimulation and then increased so that all stooling was in response to sensory awareness of a need to defecate. Each column is a month. TES was given for the months marked as 1st and 2nd. Post RX= month post TES treatment.

We have just completed a prospective study treating 68 children with STC with home-based TES. In this study, the children were previously naïve to electrical stimulation and had not had treatment by physiotherapists. We took a naïve clinician and taught him how to do the stimulation and then asked how many patients did it take for him to learn how to teach it to patients and learn the problems he needed to overcome. It took 6 patients before he had all aspects of the treatment performed reliably by the patients and also got all of their data reported to him. All the patients in this study had STC identified by a radionuclear transit study before stimulation and many had a repeat study after 6 months of stimulation. Based on previous results, patients were divided into those with <3 defecation/week and >3 defecation/week at the start of the study. Preliminary results of 32 STC children treated with
home TES (1 hr daily for 3-6 months) showed increased defecation frequency (Figure 7), reduced soiling, increased urge to defecate (Figure 8), improvement in colonic transit (Figure 9) and reduced use of laxatives [81]. Results of the larger group will be available in mid 2012.

We have found that some children with TES have delayed gastric emptying on gastrointestinal transit scintigraphy. Daily TES at the level of the umbilicus improved gastric emptying in STC children with delayed emptying. This suggests that TES may be possible as a treatment option for patients with gastroparesis or delayed gastric emptying.

Figure 9. TES daily increased the rate of colonic transit. Change in position of radioactive tracer in colon of a child (A) before TES and (B) after 6 months TES (daily at home). Images taken at 6, 24, 30 and 48 hours after ingestion of radio-isotope. This child has extremely slow transit. Before stimulation, tracer only reaches to the top of the ascending colon at 48 hrs. After 6 months of TES, the tracer reaches recto-sigmoid, with the majority of the tracer at the end of the transverse colon at 48 hours.

Home TES is well accepted by STC children/families. To assess the end-users’ views to this new method of treatment, 36 STC children/families treated with home-based TES were assessed by questionnaires assessing: rating of the treatment, time consumption, daily routine disruption; feasibility of delivery; symptom improvement, reduced laxatives used; willingness to recommend TES to other children with chronic constipation and their views on the ease of use of the device. Twenty-five/36 STC children/families responded to the questionnaires (13 males, ages:3-18yrs, mean:9yrs). All these patients had long established chronic constipation (CC). Four % had chronic constipation for <2yrs, 80% for 3-10 yrs and 16% for >10yrs. Most (64%) had a diagnosis of STC made after consulting 3-10 doctors, 28% after <2 doctors’ consultation and 8% after visiting >10 doctors. Twenty four percent had no change in symptoms. Symptom improvement developed in 76% (with 24% for <3 months, 40% lasting 3-6 months and 12% lasting >6 months). Forty-four percent of children had reduced laxatives use, with 16% unchanged and 40% unsure about the effect. Eighty-four % rated the treatment useful, while 16% were unsure about this new treatment. Ninety-six percent would recommend TES to other children with CC and 68% would purchase a machine for booster treatment if required. Devices cost $400 USD, the equivalent of 6 months of laxatives. Most families found the written instructions and personal demonstration of home TES clear and
useful. Problems with use included pads that had poor adhesiveness (72%), wire connections that broke (12%) or both (12%). All felt home TES was safe and most had minor disruptions to family routines.

There were also difficulties with using the existing device that may be overcome by training. We interviewed children who had poor response to TES to determine how they used TES. Three STC children had no response to TES and on evaluation we found they had connected the electrodes incorrectly (Figure 5E, F), so the currents were not crossed. Time was spent to educate them on the appropriate use with a protocol and a photographic reminder sent to the family at the end of the assessment. Follow-up was conducted to assess their symptoms with 3 months stimulation after the education. The symptoms assessed were soiling, defection frequency, abdominal pain, sensation of defection/urge-initiated defection and stool consistency. All 3 achieved treatment improvement with the proper use of the treatment technique. Soiling frequency decreased from 4 to 0/wk (2/3 decreased, unchanged in 1) and defection frequency increased (2/3 increased, 1 unchanged). There was an increase in urge-initiated defection and decreased abdominal pain in all 3 children. Stool consistency improved towards formed soft stool (Bristol Stool Scale 4) in all 3 children. When the response to treatment is poor, one of the important factors that requires attention is proper placement of electrodes and connection of leads. Education is a very important component contributing to successful use of this intervention.

Most of our studies have added TES on top of the patients’ existing treatment. We have also used TES at a suburban continence clinic. Following initial disimpaction, the patients are put on a structured treatment program. This includes a prescriptive diet (including high levels of fruit and vegetables with reduced processed carbohydrates), hydration (drinking at least 30 ml/kg/day, up to 1 litre/day), education on the best time to go to the toilet and the best posture to allow defection (knees raised, leaning forward), education on nervous control of the bowel and the importance of the brain/gut axis (stress affects the bowel) and given controlled laxative (stool softener and stimulant) use. TES was applied for 8-10 weeks. During this time, laxatives were reduced. This combined treatment enables the colon to return to normal function. The patients were closely monitored daily using an interactive online diary. Indications are positive with many patients becoming treatment free and symptom free within 4-6 months. We are performing a formal trial to test how much TES adds to the effectiveness of the combined treatment program.

At our institution, prior to having TES as a treatment, children were given appendicostomies and antegrade continence enemas for treatment [35]. This treatment successfully managed their condition. Since using TES, we have reduced the number of appendicostomies performed in the last 5 year period (Figure 3B). Patients were only given appendicostomy if they failed to respond to TES [82]. We have tested TES on children aged 8-18 years. We have treated a few younger children with success. It is possible that TES use on younger children will prevent them developing lifelong constipation.

**WHAT IS THE MECHANISM OF ACTION**

TES is a non-specific electrical stimulation, so many tissues or organs may be affected. TES may affect electrically-excitable cells, such as the interstitial cells of Cajal, that are
responsible for generating the slow-wave electrical activity in the bowel wall, or the nerves of the enteric nervous stimulation. Due to the close proximity of the posterior electrodes to the spinal cord (Figure 10), the spinal nerves may be affected, potentially causing upregulation of parasympathetic activity, or downregulation of sympathetic activity. It is possible that the smooth muscle of the colon may be affected in response to TES. Slow development of improvement suggests that cellular or hormonal systems are altered that produce effects long after treatment.

Figure 10. What nerves could be stimulated? The electrodes are placed on the back and belly and connected so the currents cross. The two back electrodes are either side of the spine and over the spinal outflow and the sympathetic ganglia. The current is thought to penetrate deeply and could activate the enteric neurons within the colon. In the colon it could also affect interstitial cells of Cajal and smooth muscle cells.

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<td>• Many STC children have &gt; 3 defecation / wk</td>
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<td>• Many STC children lack sensory input and have no urge to defecate</td>
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<td>• Many STC children have soiling</td>
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<td>• Many STC children have upper gastro-intestinal dysmotility</td>
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<td>• improves QOL (physical and psychosocial)</td>
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<td>• has no effect on 1/3 of patients</td>
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<tr>
<td>• may be more effective if combined with other treatments such as dietary improvement, hydration, education about the brain/gut axis and disimpaction</td>
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**FUTURE STUDIES**

Figure 11. TES produced wet stools in healthy piglets. A. Electrodes were placed on the back and abdomen of 4-week-old pigs. Stimulation was given for 30 min/day. B. Stools from sham stimulation pigs were solid and maintained their shape in the tube. Stools from pigs given active stimulation were soft and ran down the side of the cage. When placed in the tube they collapsed into the bottom of the tube. C. Wetness of stool was determined by measuring the wet and dry weight of the stools. Stools were collected before, during and after 2 weeks’ stimulation. The period of stimulation is shown with a black bar. Stool water content decreased steadily in the sham animals. Stool water content in the active stimulation animals increased in the first week and then returned to normal levels, suggesting homeostatic mechanisms have overcome the effects of the stimulation. D. Mean (SEM) water content of stools from sham and active stimulation animals. Mean value of stools collected over the 4 weeks for each group of animals. N=6 animals in each group.

We are now developing a large animal model to test the effects of TES and investigate the mechanism of action. We measured total intestinal transit of blue dye in young (4-7 week-old) piglets and water content in stools in response to TES. Our preliminary results showed that water content of stools increased (n = 6 pairs, P<0.001) and the greatest changes to water content were seen within 2 to 3 days of a daily, half-hour session of TES (Figure 11).

After 5 days of daily TES, stool water content returned to normal in healthy pigs. Total intestinal transit time measured using blue dye did not change after 2 weeks TES. We are currently using sitz-markers and x-rays to measure total intestinal and segmented intestinal...
transit (stomach, bowel and the rectum). In addition, we are developing a model of constipation in young piglets using loperamide. Opiates cause constipation as a side-effect; loperamide is a mu-opioid receptor agonist that causes constipation, but does not have any central effects. We want to test if TES can overcome opiate-induced constipation.

We have trialled TES on 10 children with anorectal retention with positive results. We are currently performing an RCT on 100 children with anorectal retention. If successful, this will provide a treatment for the larger group with chronic constipation.

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