TRANSCUTANEOUS ELECTRICAL STIMULATION TO TREAT CONSTIPATION AND FAECAL INCONTINENCE IN CHILDREN

Submitted by

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ABSTRACT

Disorders of bowel function and control are common during childhood. Children who have not gained continence, or who become incontinent past an acceptable age have decreased quality of life and behavioural co-morbidities. In this thesis, the focus is on the most common bowel dysfunction in children, namely constipation, and the role of physiotherapy in the management of this condition.

A systematic review of the efficacy of non-pharmacological, non- surgical and non-behavioural treatments of functional chronic constipation in children was undertaken. Results found preliminary evidence for the use of acupuncture and transcutaneous electrical stimulation.

A randomised sham-controlled trial on the use of interferential current in the treatment of childhood Slow Transit Constipation (STC) was then undertaken. Results found significant changes in colonic transit time, decreased soiling and abdominal pain and increased self-perceived quality of life in the treatment group compared to the sham treatment group. The question of whether comparable results could be achieved with a home –based and cheaper machines led to a pilot study of portable interferential current compared to the use of TENS. The results were inconclusive but provided preliminary data upon which to base a future randomised controlled trial.

Finally, a parallel study was undertaken to investigate the musculo-skeletal characteristics of children with STC compared to a group of children with typical development and no STC. The results showed that children with STC have reduced trunk control and posture, which indicates that physiotherapists should focus on training of trunk muscles and correction of sitting posture.

In conclusion, neuromodulation of bowel motility by electrical current is a promising treatment for children with STC.

STATEMENT OF AUTHORSHIP

Except where reference is made in the text, this thesis contains no material published elsewhere or extracted in whole or in part from a thesis submitted for the award of any other degree or diploma.

No other person's work has been used without due acknowledgement in the main text of the thesis.

The thesis has not been submitted for the award of any degree of diploma in any other tertiary institution.

Chapters 2, 3 and 5 of this thesis present papers that involved the collaboration of the authors listed.

Chapter 2 presents a systematic review which was carried out by Janet Chase with the advice and reviewing of the manuscript by Dr Nora Shields.

The concept of the studies presented in Chapters 3, 4 and 5 was that of the author of this thesis. Professor V Robertson, Professor A Catto-Smith and Professor J Hutson and Dr Bridgit Southwell wrote the application for the grant from the National Health and Medical Research Council of Australia and oversaw the research. Generation, collection, assembly, analysis and/or interpretation of data was done by Janet Chase with assistance from Dr Melanie Clarke and Dr Susie Gibb. Musculo-skeletal data were collected by Janet Chase and measurement of photographs and analysis was made with the assistance of Dr Barry Stillman. Drafting and revision of the manuscripts for these two chapters was done by Janet Chase with all authors approving the final version of the manuscript.

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CHAPTER 1: INTRODUCTION

1.1 Overview

Disorders of bowel and bladder control are common during childhood in all cultures. Of seven year-olds, ten percent wet at night, two to three percent have daytime urinary incontinence (Bower, Moore, & Shepherd, 1996) and one to four percent have faecal incontinence (von Gontaard & Neveus, 2006).

Often bowel and bladder dysfunction co-exist. The genitourinary and gastrointestinal tracts are interdependent, sharing the same embryological beginnings, pelvic location, aspects of innervation and passage through the levator ani. Commonly stool retention or constipation, with or without faecal incontinence coexists with disorders of bladder storage and emptying, both of which can lead to urinary incontinence. It is necessary to treat the underlying bowel dysfunction as well as directly addressing the bladder problem.

Children who have not gained, or who have lost continence past an age at which their care-givers expect them to do so suffer embarrassment, decreased quality of life, social limitations and behavioural co-morbidities and in the past, reactions to these conditions have varied from supportive and understanding to punitive (von Gontard & Neveus, 2006). In some medical courses childhood incontinence was taught under psychiatric conditions and treatment by a psychologist was often recommended. Although some misconceptions still prevail, childhood incontinence is now regarded primarily as a medical condition, and assessed and treated accordingly. In this thesis, the focus is on the most common bowel dysfunction in children, namely constipation, and the associated faecal incontinence.

1.2 Childhood constipation

1.2.1 Prevalence

Constipation occurs in around 3% of children and accounts for 3-5% of visits to paediatricians and 10-25% of referrals to gastroenterologists (Milla, et al., 2002; Sondheimer, 2002; Villarreal, et al., 2001; Youssef & Di Lorenzo, 2001). A positive family history can be found in 28-50% of constipated children and a higher incidence has been reported in monozygotic compared with dizygotic twins.

Constipation increases with age and there is a higher prevalence of constipation in boys with a ratio of 3:1 (Catto-Smith, 2005). In 30% of children the condition persists into adolescence and adulthood (Proctor & Loader, 2003; van Ginkel, et al., 2003).

1.2.2 Definition of constipation

There is much discrepancy concerning the definition of constipation. In part, this is due to the wide range of what is perceived as a normal stooling pattern. Definitions can be based on stool frequency, stool consistency, ease of defaecation and associated symptoms such as faecal incontinence, bloating and abdominal pain. The two most widely accepted definitions of constipation in children are those derived by the Paris Consensus on Childhood Constipation Terminology Group (Benninga, et al., 2005) and the Rome 111 criteria (Rasquin, et al., 2006) (Table 1.1).

Table 1.1 Diagnostic criteria of constipation in children

Paris Consensus on Childhood Constipation Terminology (PACCT) Group	Diagnostic criteria for Functional Constipation in Children (Rome III)
• More than one episode of faecal incontinence per week	• Two or fewer defaecations in the toilet per week
• Presence of large stools in the rectum or palpable on abdominal examination	• At least one episode of faecal incontinence per week
• Passing large stools that may obstruct the toilet	• History of retentive posturing or excessive volitional stool retention
• Display of retentive posturing and withholding behaviours	• History of painful or hard bowel movements
• Painful defaecation	• History of a large faecal mass in the rectum
	• History of large diameter stools that may obstruct the toilet
	Must include two or more of the above items, in a child with a developmental age of at least 4 years
	Accompanying symptoms may include irritability, decreased appetite and/or early satiety. The accompanying symptoms disappear immediately following passage

A normal bowel habit is defined by the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (2006) as "*having between 3 movements a week and 3 movements a day with stools that are brown or golden brown and formed, with a texture similar to peanut butter, and a size and shape similar to a sausage*". However the frequency of defaecation will also vary with age and, in babies, with how they are fed (Fontana, et al., 1989) (Table 1.2).

Table 1.2 Age related frequency of stooling in children

• 0-3 months (breast fed)	5-40 motions/week	2.9 motions/day
• 0-3 months (formula fed)	5-20 "	"
• 6-12 months	5-28 "	"
• 1-3 years	4-21 "	"
• >3 years	3-14 "	"

Faecal incontinence (organic or functional) is defined as "the passage of stools in an inappropriate place" and replaces "encopresis" or "soiling". Functional faecal incontinence is either constipation-associated, which is more common, or non-retentive - as in a child who shows no evidence of constipation.

1.2.3 Aetiology of childhood constipation

Constipation is also either organic or functional in origin, with the majority of children having no organic basis for their symptoms (Youssef & Di Lorenzo, 2001). Organic causes of childhood constipation include congenital anatomic or structural defects, metabolic and endocrine disorders, neurological disorders, connective tissue disorders, gastrointestinal disorders, cystic fibrosis and medications (Table 1.3). Any child with ongoing constipation should have an organic cause for their constipation excluded before a diagnosis of functional constipation is made.

Table 1.3 Causes of constipation in children

Congenital anatomic or structural defects
imperforate anus or anal stenosis
anteriorly displaced anus
meconium plug syndrome
Hirschsprung's disease
pelvic mass
abnormal abdominal musculature - prune belly, gastroschisis, Down syndrome
Metabolic and endocrine disorders
diabetes insipidus
hypercalcaemia and hypokalaemia
renal tubular acidosis
hypothyroidism
dehydration
multiple endocrine neoplasia type 2B
Chronic intestinal pseudo-obstruction
Cystic fibrosis
Connective tissue disorders - scleroderma, systemic lupus erythematosus, Ehlers-Danlos syndrome
Coeliac disease
Neurologic causes
damage to the spinal cord - meningomyelocele, trauma, surgery, tumours, cauda equina syndrome and tethered cord
cerebral palsy
infectious polyneuritis
amyotonia congenita
muscular dystrophy
degenerative disorders
neurofibromatosis
Cow milk intolerance or other food allergies
Other organic causes
colonic dysmotility (Slow Transit Constipation - STC)
outlet obstruction (Functional Faecal Retention - FFR)
Dietary- poor fibre or fluid intake
Medication
analgesics (Codeine preparations)
antacids
anticholinergics
anticonvulsants
tricyclic anti-depressants
β-blockers
iron and calcium supplements
antispasmodics
diuretics
Behavioural causes
learned pattern of defaecation (can be due to previous painful defaecation)
adverse life event
defiant behaviour
intellectual disability

Functional constipation is diagnosed in children where there is no objective evidence of an underlying pathological condition. The majority of children with functional constipation have either a dietary cause for their constipation, functional faecal retention or both. Children with functional faecal retention exhibit a stool-withholding pattern of defaecation. It is believed that this pattern develops due to previous painful defaecating experiences that lead to voluntary withholding of faeces in order to avoid further painful defaecation (North American Society for Pediatric Gastroenterology, Hepatology and Nutrition, 2006; Youssef & Di Lorenzo, 2001). It is estimated that up to 63% of children with constipation and soiling have had a history of painful defaecation which began when they were under 3 years of age (Partin, Hamill, Fischel, & Partin, 1992).

Alternatively, the initial insult can be as a result of toilet training, changes in routine or diet, stressful events, intercurrent illness, perianal irritation (nappy rash or group A, β-haemolytic streptococcus infection), unavailability/dislike of toilets or postponement of defaecation due to lack of interest or attention. This results in prolonged faecal colonic stasis leading to wider and firmer stools, the passage of which causes pain. Faecal incontinence is the result of looser faecal matter trickling around retained, hardened faeces. The rectum accommodates to the constant stimulus of a faecal mass and the normal urge to defaecate is lost. With prolonged distension there is decreased rectal sensation so the child may be unaware of rectal contents and faecal incontinence.

1.2.4 Treatment-resistant constipation

Seventy percent of children presenting with constipation will respond to treatment within 2 years (Staiano, Andreotti, Greco, Basile, & Auricchio, 1994; Youssef & Di Lorenzo, 2002). Thirty percent of children with constipation fail to respond to treatment and are said to have treatment-resistant or "chronic" constipation. Until recently, it was believed that most children with treatment-resistant constipation had a functional or behavioural basis for their symptoms (Robinson & Roberton, 2003). We now know that a definite population of children with chronic constipation have a condition called slow transit constipation (STC).

1.2.5 Slow transit constipation (STC)

Idiopathic slow transit constipation (STC) describes a clinical syndrome characterised by intractable constipation that is not readily responsive to laxatives, diet or a change in lifestyle

(El-Salhy, 2003). It is characterised by delayed colonic transit without an underlying systemic disorder or pelvic floor dysfunction. Although it was initially described in young women of reproductive age (Preston & Lennard-Jones, 1986; Watier, et al., 1983), it has now recognised as a condition affecting children of all ages (Benninga, et al., 1996). Up to 50-60% of children with chronic treatment-resistant constipation may have slow colonic transit. Recently, it has been suggested that STC may be part of a pan-enteric disorder as alterations in oesophageal motility (Reynolds, et al., 1987), gastric emptying (Reynolds, et al., 1987; van der Sijp, et al., 1993) and small bowel motility (Bassotti, et al., 1996; Panagamuwa, Kumar, Ortiz, & Keighley, 1994; Penning, et al., 2000) have been observed in some patients with STC.

1.2.6 The pathology of slow transit constipation

It is believed that in children with STC, the primary defect lies within the enteric nervous system (Southwell, King, & Hutson, 2005). Both clinical and manometric data suggest that the abnormal motility associated with STC should be considered as neuropathic in nature (Bassotti & Villanacci, 2006). The gastrointestinal tract contains its own nerve cell bodies that form an intrinsic network that is connected to the central nervous system via the vagal, coeliac and pelvic nerves. Enteric neurons have cell bodies within ganglia that lie in the myenteric or submucosal plexuses. The cell bodies have processes that penetrate the muscle layers where they release their neurotransmitters. Acetylcholine and tachykinins (including substance P) cause gastrointestinal muscular contraction whilst relaxation is initiated by the release of vasoactive intestinal peptide, nitric oxide and adenosine triphosphate.

Some studies have suggested that some patients with STC have an element of subclinical autonomic neuropathy (Altomare, et al., 1992; Knowles, Scott, & Lunniss, 2001; Raethjen, et al., 1997), in particular, selective small fibre neuropathies (Raethjen, et al., 1997). The same authors hypothesise that STC occurring in women post childbirth, or following pelvic surgery, may be as a result of pelvic nerve injury and that in a subgroup of people, STC should be considered a disorder of pelvic autonomic nerves (Knowles, et al., 2001).

It was with the advent of immunohistochemistry that abnormalities in the enteric neurotransmitters and neuropeptides (substance P, vasoactive intestinal peptide, nitric oxide synthase, neuropeptide Y and 5-HT) were first reported. However, findings have been inconsistent with decreased, increased and unchanged levels all being described. Although these findings could suggest that alterations of enteric neurotransmitters do not play a major role in the pathophysiology of STC, it is more likely that STC represents a heterogeneous group of disorders with the same end result - delayed colonic transit.

Although they were discovered in 1893 (Cajal, 1893), it is only relatively recently that the true importance of interstitial cells of Cajal was finally recognised. Interstitial cells of Cajal are found in the tunica muscularis throughout the gastrointestinal tract and lie between enteric nerve terminals and smooth muscle (Hagger, Gharaie, Finlayson, & Kumar, 1998; Rumessen & Thuneberg, 1996; Thuneberg, 1982; Tong, Liu, Zhang, & Zhang, 2004; Tong, Liu, Zhang, Zhang, & Lei, 2004). Their precise role has remained undetermined for several decades, however it is now thought that they act as a conduit for active transmission of electrical slow waves as well as serving as gastrointestinal pacemaker cells. A loss of the interstitial cells of Cajal has been demonstrated in a range of gastrointestinal motility disorders including STC and chronic intestinal pseudo-obstruction (Garcia-Lopez, Garcia-Marin, Martínez-Murillo, & Freire, 2009).

1.2.7 Diagnosis of constipation

Clinical

Medical history and physical examination are essential when diagnosing constipation and a thorough history should be obtained. It is important to clarify what each individual family defines as “constipation” by determining the occurrence of specific symptoms and their frequency. Essential information includes an accurate gastrointestinal and general medical assessment as well as a developmental and psychosocial evaluation. A thorough physical examination is essential in the initial assessment of a child with constipation. This should include a general examination as well as an abdominal examination and external examination of the perineum and perianal area. A rectal examination may be performed by an appropriately experienced practitioner. Blood samples should be obtained for coeliac disease screening, thyroid function testing and allergy testing (cow’s milk protein intolerance and high percentage of eosinophils in full blood count).

In most cases, a comprehensive history and examination can determine whether or not an organic cause is responsible for the constipation. If the constipation is believed to be non-organic, sufficient information can rarely be obtained in order to distinguish STC from functional faecal retention.

Diagnostic tests

Abdominal X-ray

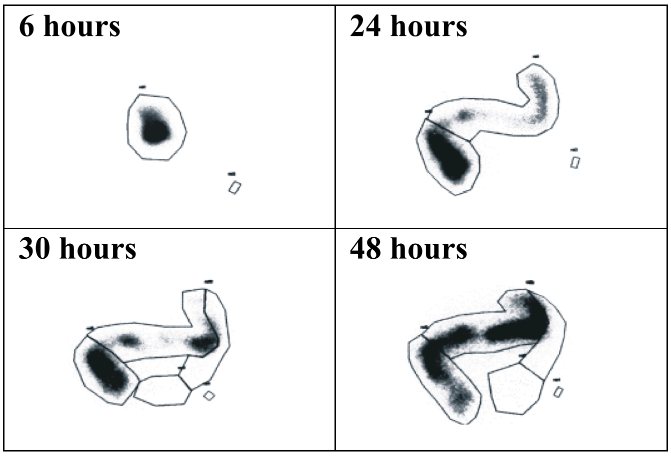
Plain abdominal x-rays have debatable value in the assessment of constipation (Catto-Smith, 2005). If faecal impaction or loading is obvious on rectal or abdominal examination then little more information can be attained by means of a plain x-ray. On rare occasions, an x-ray is useful to identify a vertebral anomaly (e.g. sacral agenesis). Abdominal x-rays can be used to assess the presence and degree of abdominal loading, especially in obese subjects or in those in whom a rectal examination is refused or inappropriate. However, interpretation of these x-rays can be subjective and x-ray timing in relation to defaecation can be misleading.

Transit Studies

Colonic transit time takes between 1-3 days during which time there is extensive mixing of bowel contents. The quantification of transit time demonstrates the presence of constipation and provides an objective evaluation of faecal clearance. Transit time has traditionally been measured using plastic, non-absorbable radio-opaque markers with transit time in different regions being determined by the ingestion of different shaped markers over 3-6 days. Studies measuring normal transit in children give the upper range of total colonic transit from 46-62 hours (Wagener, Shankar, Turnock, Lamont, & Baillie, 2004). Transit rates in children less than 5 years old are faster, while children aged 6 years or more have a range of transit and frequency of defaecation similar to adults.

This mode of assessment of gastrointestinal transit time is widely available and until recently has been considered the gold standard. However, it has now been recognised that indigestible solid particles do not move with a meal, and may not be handled by the colon in the same manner as stool (Nam, et al., 2001). Consequently, gastrointestinal transit is increasingly being investigated using scintigraphy (nuclear transit study). A tracer dose of technetium, or gallium, in 20ml of milk is ingested and images obtained at 0-2 hours to assess gastric emptying and a further image at 6 hours to ascertain whether or not the tracer has reached the colon. Subsequently, images are obtained at 24, 30 and 48 hours to document transit through the colon. The colonic transit index can be obtained based on the geometric mean of intestinal activity at 6, 24, 30 and 48 hours post-ingestion of the tracer. By this means, patients with small bowel, right, left or pan-colonic or pan-intestinal transit deficits can be distinguished from those with normal gastrointestinal transit with functional faecal retention (Figure 1.1).

(a)



(b)

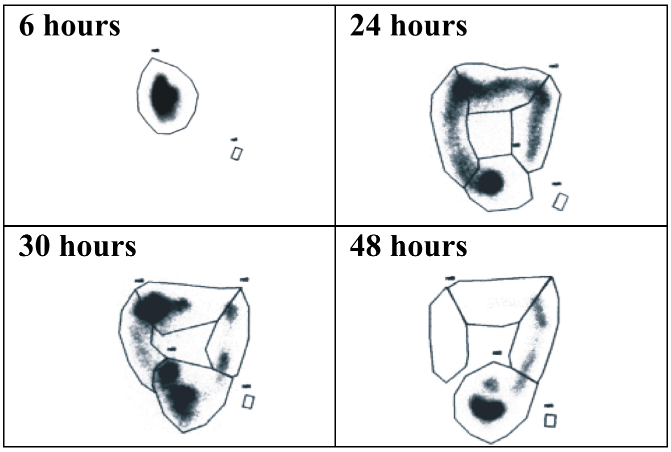


Figure 1.1 - **Nuclear transit studies demonstrating (a) slow transit constipation and (b) functional faecal retention.**

Rectal Biopsy

In cases of intractable constipation with a history of delayed passage of meconium or symptoms since birth, a diagnosis of Hirschsprung's disease needs to be eliminated by performing a rectal biopsy. Biopsy specimens are obtained from approximately 3cm above the anal verge and should be deep enough to include adequate submucosa. A diagnosis of Hirschsprung's disease is supported by an absence of ganglion cells, usually in the presence of hypertrophied extrinsic nerve fibres, with a marked increase in acetylcholinesterase activity in the lamina propria and muscularis mucosa. A rectal biopsy is also useful in identifying those children with a food allergy, as recognised by increased eosinophils in the mucosa.

Laparoscopic colonic biopsies

Recently, in children with proximal colonic delay demonstrated by their transit study, laparoscopic seromuscular biopies are being performed in association with rectal biopsy in an attempt to identify any consistent histological anomalies. Biopsies are collected from the hepatic flexure, midtransverse colon, splenic flexure and sigmoid colon without the need for suturing the defect. Specimens are processed for immunofluorescence histochemistry and are stained for substance P, vasointestinal peptide, nitric oxide synthase and cKit (a marker ICC). It has been proposed that some children with STC have a form of intestinal neuronal dysplasia, which represents an abnormality of intestinal innervation that is more subtle than Hirschsprung's disease and can be diagnosed by abnormal immunohistochemistry (Hutson, Chow, & Borg, 1996; Hutson, et al., 1997; Stanton, et al., 2003).

Colonic manometry

Colonic manometry involves the in vivo measurement of changes in intraluminal pressure within the colon. A multi-channel water-perfusion or solid-state pressure recording catheter is sited in the colon in either a retrograde manner, via colonoscopy, or an antegrade manner, via a pre-existing appendix stoma or via a naso-colic route (Figure 1.2).

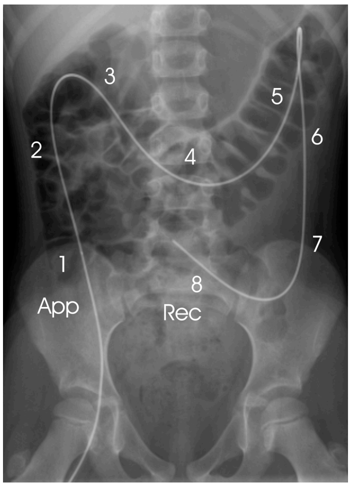


Figure 1.2 - Abdominal radiograph showing an antegradely inserted 8 channel manometry catheter passing percutaneously through the appendix (App) to the rectum (Rec) with the position of the side holes shown.

Colonic contractile activity produces changes in intraluminal pressure seen as a deviation from the baseline. Contractions can be non-propagating or propagating; propagating contractions are either in an antegrade or a retrograde direction. High amplitude contractions (>116mmHg) are thought to represent mass movement within the colon. Standards for colonic manometry in children have been defined and parameters measured. Expected frequency of propagating sequences, ratio of antegrade to retrograde contractions, frequency of high amplitude propagating sequences, post-prandial response and diurnal variation have all been determined.

1.2.8 Treatment of constipation

Seventy percent of children with constipation will respond to treatment within 2 years (Staiano, Andreotti, Greco, Basile, & Auricchio, 1994). Conventional management consists of education, dietary modification, laxatives, stool softeners, bulking agents and behavioural modification including a toilet programme. Such management may involve several members of a team of health professionals to enable specialist input and regular review and supervision of any programme undertaken.

Education

Before any therapy is initiated, it is essential to adequately educate the child (in an age-appropriate manner) and their family with regard to the cause of constipation and how often it occurs. It is also important they understand that soiling, as a result of overflow incontinence, is neither a wilful or defiant action nor a result of bad parenting. The aim is to remove blame and guilt and defuse any tensions within the family so improving motivation and compliance. Discussing the time frame of treatment is necessary so that expectations of a “quick fix” are eliminated and disappointment and disillusionment avoided. It may be necessary to reinforce educative measures several times during a management programme and supervision and problem-solving are an important aspect of care.

Dietary modification

The most common dietary cause of constipation is a low fibre diet. Within the GI tract, soluble fibre dissolves easily in water and takes on a soft, gel like texture, while insoluble fibre passes through in an almost unchanged state. By behaving in this way, fibre acts as a natural stool softener and bulking agent. There are data to suggest that increasing dietary fibre intake is beneficial in the treatment of childhood constipation (Badiali, et al., 1995; North American Society for Pediatric Gastroenterology, Hepatology and Nutrition, 2006; Loening-Baucke, Miele, & Staiano, 2004; Voderholzer, et al., 1997).

Although an increased fluid intake will not in itself relieve constipation, it is commonly believed that an increased intake of water can provide some symptomatic benefit. An increased water intake is thought to increase faecal water content and produce stools that are softer and easier to pass. Although increasing fluid intake is widely practiced, data are anecdotal and controlled trials have been unable to demonstrate any measurable difference in stool consistency (Chung, Parekh, & Sellin, 1999; Young, Beerman, & Vanderhoof, 1998).

Pharmalogical management

Before regular maintenance therapy can be commenced, it is essential to relieve any distal obstructing faeces by means of disempaction. Faecal impaction is defined as a hard mass in the lower abdomen identified during physical examination, a dilated rectum filled with a large amount of stool found during rectal examination, or excessive stool in the colon identified by abdominal radiography. Disempaction can either be performed using high dose oral laxatives or rectal therapies, or manually under anaesthetic. There have been no randomised trials comparing the efficacy of these different methods, so the choice of treatment is tailored to the individual following discussion with the patient and family.

Once the impaction has been removed then the treatment concentrates on prevention of recurrence by establishing a maintenance programme of laxatives and a toileting regime which may need to be carried out for months or years. The laxative programme is undertaken according to the needs of each child, including ease of administration, and laxatives come from the several categories, and are used singly or in combination. Commonly used laxatives are bulk forming laxatives (psyllium, methylcellulose, guar gum), emollient laxatives (mineral oil), hyperosmolar laxatives (lactulose, polyethylene glycol, sorbitol (70%), glycerine, magnesium hydroxide, magnesium citrate) and stimulant laxatives (senna, aloe, castor oil, bisacodyl, glycerin suppositories). A Cochrane review (Pijpers, Tabbers, Benninga, & Berger, 2009) concludes “that insufficient evidence exists supporting that laxative treatment is better than placebo in children with constipation”. The authors did state that compared to all other laxatives, PEG (polyethylene glycol) achieved more treatment success, but results on defaecation frequency were conflicting. They concluded that based on the results of their review, they could give no recommendations to support one laxative over the other for childhood.

Behavioural modification

Behavioural modification or habit training involves teaching a child to defaecate regularly. Toileting programmes should be developed in association with both the child and their parents in order to ensure maximum compliance. Ideally children should be encouraged to sit on the toilet for an age appropriate time (3-10 minutes) after each meal. This takes advantage of the naturally occurring gastro-colic reflex. Children should be encouraged to keep a toileting diary with suitable praise for achievable behaviours. In addition, appropriate toileting posture and muscle co-ordination should be assessed and corrected by a trained physiotherapist (Catto-Smith, 2005; North American Society for Pediatric Gastroenterology, 2006).

Some children with functional faecal retention have abnormal defaecation dynamics demonstrable by anorectal manometry. The most notable abnormality is paradoxical external anal sphincter contraction during attempted defaecation -pelvic floor dyssynergia or anismus. Biofeedback training aims to eliminate this by visually and aurally reinforcing repeated external anal sphincter relaxation until a recognisable sensation is achieved without the need for feedback.

A Cochrane review (Brazzelli & Griffiths, 2006) identified randomised and quasi-randomised trials of behavioural and/or cognitive interventions with or without other treatments for the management of faecal incontinence in children. Of eighteen trial identified results of nine trials were able to be combined and showed higher rather than lower rates of persisting symptoms of faecal incontinence up to 12 months when biofeedback was added to conventional treatment (laxatives and toileting programmes) (OR 1.11 CI 95% 0.78 to 1.58). The authors concluded that there is no evidence that biofeedback training adds any benefit to conventional treatment in the management of functional faecal incontinence associated with constipation in children. In the same review the authors identified a randomised-controlled trial of 161 children which lead them to conclude that there is some evidence that a combination of behavioural interventions and laxative therapy was better than laxative therapy alone to improve continence in children with functional faecal incontinence associated with constipation. This Cochrane review (Brazzelli & Griffiths, 2006) was edited in 2009 and the conclusions remain current.

Surgical intervention

Despite conventional management, 30% of children continue to have chronic treatment-resistant constipation which may be associated with abdominal pain, pain on defaecation, faecal incontinence, recurrent faecal impaction, megacolon, megarectum, with or without associated bladder symptoms. These children have poorly controlled symptoms, many hospital visits, poor quality of life and their parents have ongoing associated financial costs (Clarke, et al., 2008).

Until recently surgical management of chronic treatment-resistant constipation consisted mostly of bowel resection with or without formation of a stoma. Now, a less invasive approach is taken with the formation of a continent appendix stoma. This technique was first described by Malone for the management of incontinence after correction of an anorectal malformation (Malone, Curry, & Osborne, 1998; Marshall, Hutson, Anticich, & Stanton, 2001). The appendix is brought through the anterior abdominal wall, traditionally in either the right iliac fossa or at the umbilicus, and sutured to the skin to form an appendicostomy. Antegrade continence enemas are then performed via the stoma to flush faeces from the caecum to the rectum. When the colon is intermittently (every 2-3 days) washed out in this manner, it remains relatively empty and continence and soiling is improved. However, results are variable and distressing stool or mucous leakage from an appendicostomy or stomal stenosis can necessitate stomal revision (Marshall, et al., 2001).

1.3 Therapeutic electrical stimulation

The limitations and undesirable outcomes of the surgical and laxative-based treatments described above highlight the importance of developing an alternative method for treating constipation. Electrical stimulation is a commonly used and well-accepted therapeutic modality used by physiotherapists in the treatment of bladder dysfunction and urinary incontinence. It is used to inhibit detrusor overactivity (Bower & Yeung, 2004) and to facilitate detrusor contractility (Gladh, Mattsson, & Lindstrom, 2003). Four forms of electrical stimulation have previously been used to treat disorders of the gastrointestinal disorders: transcutaneous electrical nerve stimulation (TENS), interferential current (IFC), electroacupuncture and sacral nerve implantation or stimulation. It is possible that one or more of these forms of therapy might be effective in the treatment of STC in children.

1.3.1 Transcutaneous Electrical Nerve Stimulation (TENS)

TENS was initially used in clinical practice in the 1960's and introduced the concept that pain may be relieved by peripheral stimulation that can take the form of rubbing, vibration, heat, cold or, electrical stimulation. The electric stimulus is delivered at variable current strengths, pulse rates and pulse widths and usually using pre-gelled self-adhesive electrodes. The waveform is biphasic in order to avoid the electrolytic and iontophoretic effects of a unidirectional current. TENS is traditionally categorised into three forms: high-frequency, low-frequency and pulsed (burst). The most conventional form of TENS is high-frequency. The stimulus is delivered at a frequency >10Hz (usually 40-150Hz) but at a low current intensity, just above threshold, between 10-30mA. The pulse duration is short, typically around 50-250 microseconds. Low-frequency TENS delivers a stimulus of <10Hz (usually 1-10Hz), at a high current intensity, close to the tolerance limit of the patient. Pulsed TENS uses low-intensity stimuli fired in high-frequency bursts. No particular advantage of this method over conventional TENS has been described.

1.3.2 Interferential therapy/current (IFC)

Interferential current (IFC) is a form of electrical stimulation that involves the transcutaneous application, via electrodes, of two crossed, slightly out of phase, medium-frequency currents.

This produces an amplitude-modulated current effect within the tissues. As with TENS, the frequency, amplitude and pulse width of the output waveforms can be regulated. Conventionally, currents within the range of 3,900 to 4,100Hz are used, as lower frequency currents can result in somewhat uncomfortable polarisation effects in the superficial tissues. Typically a quadripolar model is adopted where four electrodes are placed over the target area, as it was thought that in such a distribution that their current paths cross directly over the relevant organ(s). This is not so (Robertson, Low, Reed, & Ward, 2006). Modulated IFC applied to the trunk will spread in many directions according to the tissue arrangement because of differences in their impedance, and unless the orientation of nerve fibres is optimal stimulus modulation may be partial (Ward, 2009).

1.3.3 Electroacupuncture

Although the Chinese have been using acupuncture for over 3000 years, it wasn't until the 17th century that it was introduced to Europe. Even then it failed to gain popularity in Western culture with the majority of people regarding it as Eastern folklore. It is only in the last 25 years that there has been a dramatic turn-around in the perceived acceptability of acupuncture. This follows the publication of long-awaited articles that finally reveal causal mechanisms for many of acupuncture's effects (Ulett, 1983). Acupuncture involves insertion of needles which are usually manually manipulated at a specific acupuncture points. Heat or moxibustion, pressure and electrical stimulation can also be used over acupuncture points. Electroacupuncture involves attaching the inserted needle to an electric pulse generator. It has been shown that conducting polymer pads are as effective as needles (Ulett, Han, & Han, 1998) so cutaneous stimulation (without skin penetration) using TENS over acupuncture points is possible.

1.3.4 Sacral Nerve Stimulation

A new form of stimulation had been created that involves extradural stimulation within the sacral canal and is utilised in the management of urinary and faecal incontinence and chronic pelvic pain. Following acute peripheral nerve evaluation to locate the optimal sacral spinal nerve that will elicit contractions of the striated pelvic floor muscles (usually S3), patient's progress to sub-chronic peripheral nerve evaluation for a minimum of 7 days to assess the relative efficacy of sacral nerve stimulation. If a clear benefit is perceived then a permanent implantable device can be inserted. Adoption of this route of administration of electrical therapy has dramatically reduced the incidence of complications and this had led to a more widespread adoption of sacral nerve stimulation.

1.3.5 Electrical stimulation in the treatment of gastrointestinal disorders

As far back as 1913, studies have reported the effect of electrical stimulation of somatic afferents from skin and muscle on gastrointestinal tract motility in dogs, cats and rats (Takahashi, 2006). More recent studies been carried out on healthy adult human volunteers and people with specific dysfunctions of the gastrointestinal tract. Presented below are some of the later studies relating to the effect of electrical stimulation on motility of the gastrointestinal tract. The participants are adults unless otherwise stated.

Camilleri, Malagelada, Kao, & Zinsmeister (1984) undertook an experimental study aimed at investigating somatovisceral reflexes previously studied in animals. TENS was applied to eighteen healthy human volunteers while simultaneously monitoring their upper gastrointestinal phasic pressure activity, extraintestinal vasomotor indices, and plasma levels of accepted humoral mediators of autonomic reflexes. Painful stimuli were applied either to the hand (C8-T1) or to the upper abdomen (T5-T10) to determine whether impulses at these two dermatomes produced different effects. Participants received active or sham stimulation at either of the two sites. A significant reduction (p = 0.007) in the antral motility index when TENS was applied to the hand and abdomen as compared with sham stimulation was noted. An associated increase in skin conductance and plasma beta-endorphin levels was described but no change in pulse, blood pressure, or circulating catecholamine levels. It was concluded that the similarity of the responses to TENS applied to the hand and abdominal dermatomes suggested that the induced somatovisceral responses relay predominantly at the cerebral level.

TENS and achalasia

Achalasia is a disorder of the oesophagus in which there is a failure of the lower oesophageal sphincter to relax during swallowing. In addition, there is an abnormality in oesophageal motility and a high resting pressure of the lower oesophageal sphincter. Vasoactive intestinal peptide is believed to be the inhibitory neurotransmitter responsible for relaxation of the lower oesophageal sphincter. In patients with achalasia, the concentration of vasoactive intestinal peptide and the number of vasoactive intestinal peptide -containing nerve fibres are reduced or absent. The effect of TENS on oesophageal function has been assessed in normal subjects (Chang, Chey, & Ouyang, 1996) and as a treatment for people with achalasia (Guelrud, Rossiter, Souney, Mendoza, & Mujica, 1991; Guelrud, Rossiter, Souney, & Sulbaran, 1991; Mearin, Zacchi, Armengol, Vilardell, & Malagelada, 1990; Sallam, McNearney, Doshi, & Chen, 2007)

In one study involving patients with achalasia, the pressure of their lower oesophageal sphincter, along with their vasoactive intestinal peptide levels, were measured before and after treatment (Guelrud et al., 1991). The authors reported that there was a statistically significant reduction in the lower oesophageal sphincter pressure after only 45 minutes of treatment at low-frequency (6.5Hz), stimulating C8, T1 with electrode placement on the dorsum of the hand between 1st and 2nd metacarpal bones and ulnar border of same hand This reduction was further increased after a week of daily treatment.

Ninety percent of patients with systemic sclerosis or scleroderma report mild to significant gastrointestinal symptoms usually attributed to hypomotility of the gut, and the prevalence of disturbances of gastric myoelectric activity is 80-90%. A study that looked at oesophageal motility and lower oesophageal sphincter pressure in patients with achalasia and scleroderma (Mearin, et al., 1990), reported that there was no detectable changes in oesophageal motility following administration of either low or high frequency TENS also to the hand. In a high quality study carried out by Sallam et al. on patients with scleroderma (Sallam, et al., 2007), an improvement was noted particularly in oesophageal symptoms after prolonged use of TENS (two weeks) but not acute TENS (30 minutes), which may explain the conflicting results between these two studies.

Electrotherapy for delayed gastric emptying

Gastric myoelectrical activity can be measured by cutaneous electrogastrography (Hamilton, Bellahsene, Webster, & Bass, 1986) and abnormal recordings have been reported in a number of conditions including diabetic gastroparesis, post-operative and pregnancy-induced nausea and vomiting and motion sickness (Chen & McCallum, 1993). In a review article, Takahashi (2006) reports the above conditions have been successfully treated by means of acupuncture, electroacupuncture or acupoint TENS with success possibly resulting from an alteration in gastric electrical activity. Chang, Chou, Ko, Wu, & Chen (2002) investigated if cutaneous electrical stimulation or electroacupuncture over Zusanli points in 15 male healthy volunteers produced any demonstrable changes in myoelectrical electrogastrography recordings. Participants were studied for three sessions in random order with three days between sessions. The sessions comprised 30 minutes of baseline recording 30 minutes of either electroacupuncture or cutaneous or sham- electrical stimulation over Zusanli (Stomach 36) acupuncture points, and 30 minutes of post-intervention recording. The results were that electroacupuncture and cutaneous electrical stimulation provoked a significant increase in the percentage of normal frequency gastric electrical activity with concomitant decreases in the percentages of periods of tachygastric and bradygastric rhythms compared to sham group. These findings led the authors to the conclusion that transcutaneous Zusanli electrical stimulation has the ability to enhance the regularity of gastric myoelectrical activity. These findings supported the earlier work of Lin et al. (1997) who studied 9 healthy humans with electroacupuncture over Stomach 36 and Pericardium 6. Both studies eliminated confounding factors such as medication use and any conditions which may affect gastric motility, but Lin et al.(1997) did not use sham stimulation and part of their study protocol.

Weinkauf, Yiannopoulos, & Faul (2005) describe two case reports of patients with post-lung-transplant gastroparesis due to a presumed vagus nerve injury during their operations. The first patient who was having TENS for back pain 18 months post-transplant was noticed to have a marked improvement in his gastric emptying following his electrical therapy. The authors proceeded to apply paraspinal TENS to another patient with persistent gastroparesis some 8 months post-transplant. The electrodes were placed over T3 and T12, each covering the paraspinal areas bilaterally. After a treatment period of 20-30 days her symptoms had also completely resolved. Previously gastric pacemaker insertion had been reported to improve gastric motility following lung transplantation (Yiannopoulis, Shafazand, & Ziedalski, 2004) indicating the potential for reversibility of the condition using electrical stimulation. Both cases described by Weinkauf et al. had gastric scintigraphy and objective evidence of gastric emptying delay prior to TENS use, but only the second case had repeat scintigraphy which showed a marked reduction in gastric emptying time as her symptoms resolved. Both patients had resolution of symptoms and discontinued pro-kinetic medication use and complete relief was maintained 6-12 months later.

TENS and irritable bowel syndrome

Irritable bowel syndrome is defined as a condition that is characterised by lower abdominal pain in association with disturbed defaecation in the absence of any organic abnormality.

Those diagnosed with irritable bowel syndrome can be further classified as having either diarrhoea-predominant irritable bowel syndrome or constipation-predominant irritable bowel syndrome. Currently the most widely accepted physio-pathological hypothesis to explain irritable bowel syndrome is the presence of dysregulation of the neurobiology of visceral neural afferents and pain sensitivity control. (Whitehead, Engel, & Schuster, 1980). There is evidence that the endogenous analgesia system is abnormal in irritable bowel syndrome patients and it is strongly suspected that levels of substance P, cholecystokinin, neuropeptide Y, and peptide YY may be related to the pathophysiology of irritable bowel syndrome (Whitehead et al., 1980).

Patients with irritable bowel syndrome often complain of abdominal pain and appear to have a lower sensory threshold to rectal distension. Recognising the potential application of electrical therapy in gastrointestinal conditions, Xiao & Liu (2003) evaluated the rectal sensory thresholds in patients with irritable bowel syndrome and assessed whether these measurements were affected by the administration of either short- or long-term acupoint TENS. The acupuncture points used were LI 4 between the thumb and forefinger, St 36 on the anterior lower leg, and UB 57 on the posterior aspect of the calf. Their initial data confirmed that patients with diarrhoea predominant irritable bowel syndrome have a significantly lower rectal sensory threshold when compared to patients with constipation predominant irritable bowel syndrome or healthy age-matched controls. Following administration of both short- and long-term TENS there was a significant elevation of rectal sensory thresholds in the participants with diarrhoea predominant irritable bowel syndrome, with patients also reporting a decrease in stool frequency and a decrease in abdominal pain.

IFC and treatment-resistant constipation

Interferential stimulation has been used for some time in the treatment of urinary urgency and urge incontinence due to detrusor overactivity. It was noted that adult patients undergoing treatment for detrusor overactivity reported a high incidence of diarrhoea following commencement of IFC. This diarrhoea is believed to be as a result of increased colonic transit due to incidental electrical stimulation of the bowel. Consequently, researchers have posed the question as to whether or not IFC could be used as a treatment modality in its own right for patients with constipation.

Chase, Robertson, Southwell, Hutson, & Gibb (2005) undertook a pilot study (n=8) investigating the effect of IFC in a group of children with treatment-resistant slow transit constipation. IFC was used in preference to TENS as it was comfortable and had the potential to produce a greater stimulation intensity at depth (Robertson et al., 2006). De Domenico (1987) claimed IFC could be used to treat 'abdominal organ dysfunction' however, no empiric evidence of IFC being used clinically to treat constipation or other abdominal problems was offered. Participants in this trial were children who had chronic constipation and soiling for a minimum of four years and had had exhaustive medical and behavioural treatment to no effect. The study found that following a treatment period of only one month (20 minutes duration, three times per week) there was a decrease in the reported incidence of soiling and an increase in the incidence of spontaneous defaecation. A subgroup of the children had previously had appendicostomies formed in order to be able to perform formal bowel washouts (n=3). This group of children reported a decreased need for bowel washouts following treatment with IFC, and two children were able to stop using their appendicostomy altogether. Although the children in this series of case studies had nuclear transit studies prior to the intervention, this objective measure was not repeated after the intervention and results were based on self-reported bowel diaries.

Sacral nerve stimulation and faecal incontinence

Sacral Nerve Stimulation has been shown to be able to improve faecal incontinence in adults due to physiological levator ani and external anal sphincter dysfunction (Vaizey, Kamm, Turner, Nicholl, & Woloszko, 1999). However Sacral Nerve Stimulation has also been shown to be of benefit to patients with neuropathic faecal incontinence, cauda equina syndrome (Rosen, Urbarz, Holzer, Novi, & Schiessel, 2001) and internal anal sphincter dysfunction (Vaizey, et al., 1999) and even patients with limited structural defects of their internal and external anal sphincters (Malouf, Vaizey, Nicholls, & Kamm, 2000). The ability of Sacral Nerve Stimulation to improve faecal incontinence due to such a diverse range of conditions highlights how little is understood of its possible mechanism of action. A number of studies have reported that Sacral Nerve Stimulation is beneficial for STC (Dinning, Fuentealba, Kennedy, Lubowski, & Cook, 2007; Malouf, Wiesel, Nicholls, Nicholls, & Kamm, 2002). Early work using Sacral Nerve Stimulation in children has shown some benefits in both urinary and faecal incontinence and constipation (Humphreys, et al., 2006; Roth, Vandersteen, Hollatz, Inman, & Reinberg, 2008).

Humphreys et al. (2006) reported on twenty-three patients (6-15 years old) whose presenting symptoms of dysfunctional voiding, enuresis, incontinence, urinary tract infections, bladder pain, urinary retention, urgency, frequency, constipation and/or fecal incontinence (often referred to as Dysfunctional Elimination Syndrome) were treated with Sacral Nerve Stimulation, and who were followed for a mean of 13.3 months after surgery.

Constipation improved in 12 of 15 patients (80%) and was unchanged in 3 (20%) postoperatively, however "improvement "was not defined, neither how it was judged. Thirteen patients still reported symptoms of constipation at the end of the trial period and four of the ten children who had faecal incontinence at the outset continued to do so.

Roth et al. (2008) treated twenty children with Dysfunctional Elimination Syndrome (DES) with Sacral Nerve Stimulation. The children kept a bowel diary and improvement was defined as an increase in the number of bowel actions per week and a decrease in the weekly number of episodes of painful defaecation. Of the 17 children (85%) with constipation at the onset of the study, 7 (41%) had resolution of constipation and 5 (29%) exhibited improvement. Although faecal incontinence is a common symptom of children with DES this was not mentioned by the authors. In both studies the majority of patients with DES experienced resolution or improvement of voiding symptoms and lead revision, infection, skin sensitivity and device failure are the documented complications.

Sacral Nerve Stimulation in children is in its infancy. In the absence of long-term prospective clinical trials comparing Sacral Nerve Stimulation to conservative management a definitive conclusion regarding efficacy cannot be made. At present it seems it should be used only on carefully selected patients in whom all other treatment has failed.

Several trials have suggested encouraging results regarding the application of electrotherapy in the management of achalasia, gastroparesis, irritable bowel syndrome, constipation and chronic abdominal pain however it has not yet been incorporated into routine management strategies for these conditions. When treating bladder dysfunction with electrical stimulation key elements are availability of inexpensive and safe machines and of staff trained to select appropriate electrical parameters, to prescribe, teach, monitor and review the treatment. Whether clinic-based or home-based treatment is available is also an issue of importance as some patients are unable to administer their own treatment, and others need daily treatment at home to gain an effect and maintain compliance.

One of the biggest problems regarding the acceptance of electrical therapy is the overwhelming lack of data concerning its precise mechanism(s) of action. Although there are many theories as to the potential effects of electrical stimulation, they remain unsubstantiated. Many sceptics believe any perceived benefits from recipients of electrotherapy are purely due to a placebo effect. Trials have attempted to eliminate this argument by blinding participants with either low-current sham stimulation or by short-circuiting half of the trial machines so that they do not deliver any current despite the dials/displays/lights functioning normally. However, both of these methods have obvious limitations. Firstly, in regard to bowel dysfunction we are unaware of how electrotherapy works, therefore we cannot be completely sure that even a low level of current may have some therapeutic action. Secondly, electrotherapy tends to result in some sort of sensory stimulation under the electrodes; this is evidently absent with a sham machine. As a result it can be argued as to whether or not participants are truly blinded to their treatment pathway. Despite this most studies (Bower et al., 2004, Gladh et al., 2003, Chase et al., 2005) have shown that improvements from electrostimulation appear to be sustained over a period of time following cessation of treatment. This is contrary to what would be expected were the effects due purely to a placebo response.

1.4 The role of the Physiotherapist in the treatment of constipation

The role of the physiotherapist in the management of constipation in the adults is well established as pelvic floor muscle training (including exercise prescription and electrotherapy), pressure and electromyographic biofeedback and retraining of the muscles used in defaecation are directly applicable to the causes of bowel dysfunction in this population. In children, this role is, as yet, not as well-defined.

In the treatment of children, the term urotherapy "means nonsurgical, nonpharmacological treatment for LUT malfunction" (Neveus et al., 2006). As such it also involves the treatment of bowel dysfunction, as the two often co-exist. A urotherapist can be a doctor, nurse or physiotherapist and ideally tertiary treatment centres have a team of health professionals available in a paediatric continence clinic. In such settings teams evolve and members have shared skills. There are also discipline-specific skills which can enhance the overall approach to assessment and treatment. For example, being a physiotherapist having experience of using electrical current to influence bladder behaviour leads to thoughts regarding its application to bowel motility in children who have not responded to other treatments. The discipline of observing postural characteristics and movement leads to the observation of joint hypermobility and characteristic postural habits in children with constipation. In this thesis it is the physiotherapy training in the use of therapeutic electrical stimulation and the observation of musculo-skeletal characteristics that have led to the research that is reported herein.

1.5 Aims of Thesis

There is a need to develop new treatments for constipation in children whose symptoms are not helped by current interventions. Electrical stimulation has been shown to have an effect on gastrointestinal motility.

The first aim of this thesis was to establish whether any treatments other than those usually prescribed for constipation (education, pharmacological, surgical and behavioural management) in children had been investigated, and if so what was the efficacy of those treatments. To achieve this, a systematic review was conducted. Details of the review are presented in Chapter 2.

The second aim was evaluate the efficacy of transcutaneous interferential current as a treatment for children with STC. Chapter 3 reports the results of a randomised placebo-controlled trial assessing the application of transcutaneous interferential electrical therapy in the management of children with chronic constipation unresponsive to at least 2 years of conventional treatment.

The third aim was to establish if the application of TENS would have the same effect as the application of interferential current in children with STC. The results of a pilot study to determine this are presented in Chapter 4.

The fourth aim was to investigate if the musculo-skeletal characteristics of children with STC were different from a group of children with no bowel dysfunction. This was done to establish if lack of control of the voluntary muscles of defaecation may be impacting on the ability to defaecate in children with STC. The results are reported in Chapter 5.

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CHAPTER 2: PREFACE

The systematic review presented in Chapter 2 has been accepted for publication in The Australian and New Zealand Continence Journal, a peer-reviewed journal of the Continence Foundation of Australia and the New Zealand Continence Association. The format has been changed from that required by the Journal to be consistent with the rest of this thesis, but is otherwise unchanged.

CHAPTER 2: A SYSTEMATIC REVIEW OF THE EFFICACY OF NON-PHARMACOLOGICAL, NON- SURGICAL AND NON-BEHAVIOURAL TREATMENTS OF FUNCTIONAL CHRONIC CONSTIPATION IN CHILDREN

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2.2 Abstract

The aim of this review was to establish the efficacy of non-pharmacological, non-surgical and non-behavioural treatments of functional chronic constipation in children.

A secondary aim was to identify any non-pharmacological, non-surgical and non-behavioural treatments of functional chronic constipation.

Electronic databases were searched for articles within the date parameters 1948 to March 2009 using the keywords and MeSH terms: constipation, encopresis, faecal, faecal, soiling, anal incontinence, inertia, colon/colonic and child/children/childhood, paediatric, paediatric, teenage, adolescent, school-age, and treatment, therapy, therapeutic, management, physiotherapy, rehabilitation, exercise, fitness, training, massage, acupuncture, stimulation, electrical, neuromodulation, electrotherapy, TENS. Using searching and citation tracking methods, additional articles were identified.

Articles were selected against the following criteria: participants aged 0-18 years, participants who had a diagnosis of functional chronic constipation for longer than 8 weeks not related to congenital abnormalities or disease, English language, and that treatment was non-pharmacological, non-surgical or non-behavioural. Of the 468 articles initially identified, 6 met the inclusion criteria and underwent detailed review.

Data were extracted from the included studies on a standardised form adapted for this review and evaluated on a checklist of quality assessment questions.

This review has shown a scarcity of literature in this area of interest and the evidence for the efficacy of the interventions identified of low quality. The treatment modalities identified were chiropractic, reflexology, acupuncture and electrical stimulation, the latter two most deserving of further well-designed research.

2.3 Introduction

Constipation occurs in around 3% of children and accounts for 3-5% of visits to paediatricians and 10-25% of referrals to gastroenterologists (Milla, et al., 2002; Sondheimer, 2002; Youssef & Di Lorenzo, 2001).A positive family history can be found in 28-50% of constipated children. Constipation increases with age and there is a higher prevalence of constipation in boys with a ratio of 3:1(Catto-Smith, 2005). In 30% of children the condition persists into adolescence and adulthood (Proctor & Loader, 2003; van Ginkel, et al., 2003).

The definition of constipation has been based on stool frequency, stool consistency, ease of defaecation and associated symptoms such as soiling, bloating and abdominal pain. The two most widely accepted definitions of constipation in children are those derived by the Paris Consensus on Childhood Constipation Terminology (PACCT) Group (Benninga, et al., 2005) and the Rome III (Rasquin, et al., 2006) criteria (see Table 2.1).

Table 2.1 Diagnostic criteria of constipation in children

Paris Consensus on Childhood Constipation Terminology (PACCT) Group	Diagnostic criteria for Functional Constipation in Children (Rome III)
• More than one episode of faecal incontinence per week	• Two or fewer defaecations in the toilet per week
• Presence of large stools in the rectum that are palpable on abdominal examination	• At least one episode of faecal incontinence per week
• Passing large stools that may obstruct the toilet	• History of retentive posturing or excessive volitional stool retention
• Display of retentive posturing and withholding behaviours	• History of painful or hard bowel movements
• Painful defaecation	• History of a large faecal mass in the rectum
	• History of large diameter stools that may obstruct the toilet
	Must include two or more of the above items, in a child with a developmental age of at least 4 years
	Accompanying symptoms may include irritability, decreased appetite and/or early satiety. The accompanying symptoms disappear immediately following passage

Faecal incontinence is defined as "the passage of stools in an inappropriate place" and has been chosen as a term to replace "encopresis" or "soiling". It can be either organic or functional in origin with functional faecal incontinence being further classified as either constipation-associated or non-retentive (that is in a child who shows no evidence of constipation by history or examination). Faecal incontinence associated with constipation is more common. The majority of children having no organic basis for their symptoms (Youssef & Di Lorenzo, 2001). Organic causes of childhood constipation, which account for less than 5% of cases, include congenital anatomic or structural defects, metabolic and endocrine disorders, neurological disorders, connective tissue disorders, gastrointestinal disorders or cystic fibrosis.

Functional constipation is diagnosed in those children where there is no objective evidence of an underlying pathological condition (see Figure 2.1A). It is estimated that up to 63% of children with constipation and soiling have had a history of painful defaecation which began when they were under three years of age (Partin, Hamill, Fischel, & Partin, 1992). Changes in routine or diet, stressful events, intercurrent illness, perianal irritation, unavailability/dislike of toilets, or postponement of defaecation due to lack of interest or attention contribute to the problem. Withholding leads to colonic stasis with increased reabsorption of faecal fluid, resulting increase in the size and firmer consistency of the stools, the painful passage of which reinforces the perceived pain of defaecation. Overflow diarrhoea or soiling is the result of watery faecal matter trickling around retained, hardened faeces. With time the rectum becomes accustomed to the constant stimulus of a faecal mass and the normal urge to defaecate is lost. This decrease in rectal sensation also means that the child is often unaware of the unintentional passage of faecal matter (see Figure 2.1B).

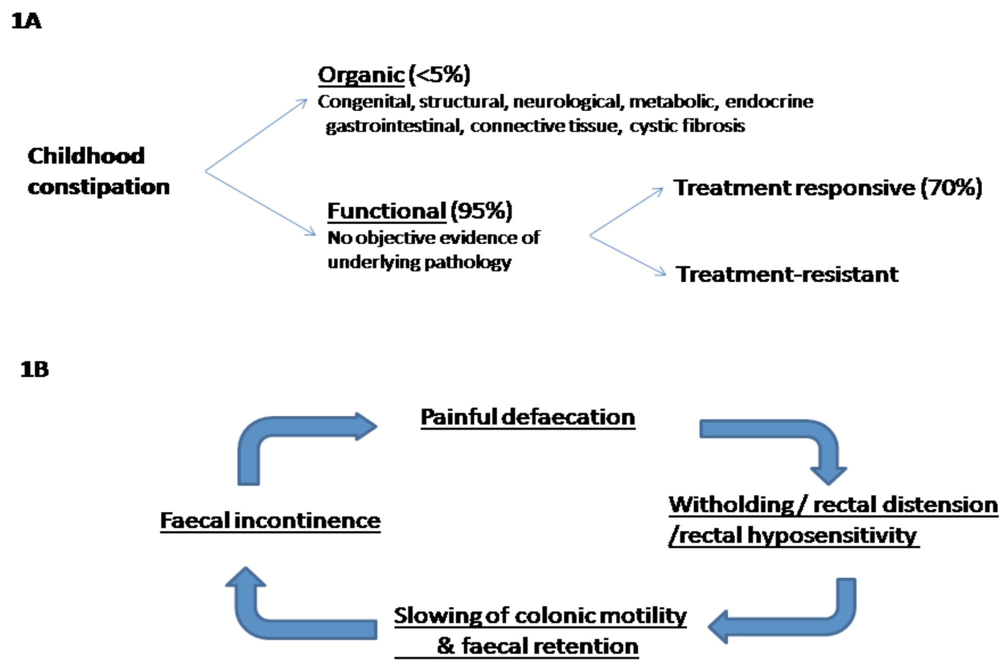

Figure 2.1 1A Simple classification of childhood constipation.
1B The painful defaecation cycle.

Management of constipation in children usually involves education, laxative regimes and behavioural modification, including toileting programmes and possibly biofeedback aimed at teaching relaxation of anal sphincter and pelvic floor muscles. After 6 months to 2 years of such management, 70% of constipated children have recovered (Southwell, King, & Hutson, 2005). However, relapse is very common. The remaining children are said to have chronic treatment-resistant constipation, which may be associated with abdominal pain, pain on defaecation, faecal incontinence, recurrent faecal impaction, megacolon, megarectum, with or without associated bladder symptoms. These children have poorly controlled symptoms, many hospital visits, poor quality of life and ongoing associated financial costs (Clarke, et al., 2008). In severe cases surgical interventions such as partial colectomy or appendicocaecostomy may be undertaken with varying results (Hutson, McNamara, Gibb, & Shin, 2001; Marshall, Hutson, Anticich, & Stanton, 2001).

Overall, there appears to be deficiencies in the evidence for current treatments of constipation in children (Brazzelli & Griffiths, 2006; Pijpers, Tabbers, Benninga, & Berger, 2009; Price & Elliot, 2001), and one third of children are non-responders to the medical, surgical and behavioural interventions currently used. This leads to the question as to whether there are any other treatments or interventions, which may be effective in the treatment of constipation in children.

Therefore the primary aim of this systematic review was to establish the efficacy of non-pharmacological, non-surgical and non-behavioural treatments of functional chronic constipation in children. A secondary aim was to identify any of non-pharmacological, non-surgical and non-behavioural treatments of functional chronic constipation, used either alone or in combination with pharmacological, surgical and behavioural interventions.

2.4 Methods

2.4.1 Search Strategy and Selection Criteria

Amed (1985 to March 2009), Embase (1998 to March 2009), Pubmed (1948 to March 2009), Medline (1966 to March 2009), CINAHL (1982 to March 2009), Cochrane library, Pedro and the Web of Science (ISI) electronic databases were searched for relevant articles. A combination of MeSH headings and free-text search-terms were used and linked by the Boolean operators (OR and AND) including: constipation, encopresis, faecal or fecal, soiling, anal, incontinence, inertia, colon or colonic, child, children or childhood, paediatric or paediatric, teenage or adolescent, school-age or schoolage, treatment, therapy, therapeutic, management, physiotherapy, rehabilitation, exercise, fitness, training, massage, acupuncture stimulation, electrical, neuromodulation, electrotherapy, TENS.

The resulting yields from each electronic database were imported into Endnote Version X2.

Additional articles were located by manually examining the reference lists of identified articles. A search was made in the databases (as listed), and on the Internet, to determine whether the authors of the included papers had published other relevant work that had been missed in the initial database searching. References of included studies and author names were tracked through the Science Citation Index.

The title and abstracts of the articles identified by the search strategy were assessed against the criteria: participants aged 0-18 years, participants who had a diagnosis of functional chronic constipation for longer than 8 weeks not related to congenital abnormalities or disease, English language, and studies of non-pharmacological, non-surgical or non-behavioural treatments such as abdominal massage, electrical stimulation, manipulation or exercise. Articles were not excluded on the basis of research design. Studies were excluded if the interventions were (either separately or in combination) education programmes, laxative regimes, toileting programmes, behavioural/educational/psychological therapies, surgery or dietary measures.

2.4.2 Data Extraction

Data were extracted from the included studies on a standardised form adapted for this review (see Appendix A) and included the following: study design, participants' gender and age, description of intervention, frequency of intervention and duration of treatment programme, outcome measures, results and adverse events.

2.4.3 Quality Assessment

Validated assessment scales such as PEDro were not applicable due to the design of the studies and so the author developed a checklist of quality assessment questions. The checklist was based on one published for use in assessing both randomised and non-randomised studies (Downs & Black, 1998). Downs and Black reported that their checklist had high internal consistency (Kuder Richardson-20: 0.89), as did the subscales apart from external validity (KR-20: 0.54). Test-retest (r 0.88) and inter-rater (r 0.75) reliability were also good. Modification of their checklist, which may have altered its reliability and validity, resulted in a seven-question list, which was applied to the identified papers (see Table 2.2). For each of the seven areas on the assessment checklist the content of the journal article was quality evaluated and awarded a score of two if the item was fully met, one if partially met and zero if not adequately met. Three reviewers independently assessed the quality of the included articles. Any differences in the articles' assigned scores between reviewers were resolved by consensus.

Table 2.2 Scoring of six articles using the author's 7-point modified criteria

Number	Criterion	Satisfied if…	Reference	Score
1	Was the objective of the study clearly stated?	The report described the aim of the study in the introduction or methods	Broide, et al. 2001	2
			Barber & Ring 2002	1
			Bishop et al. 2003	0
			Chase, et al. 2005	2
			Quist & Duray 2007	1
			Alcantara & Mayer 2008	1
2	Was the disease status of the cases reliably assessed?	The report described the assessment protocol that ensured the children had chronic constipation. This item was partially met if it stated the children were assessed but did not describe how	Broide, et al. 2001	2
			Barber & Ring 2002	0
			Bishop et al. 2003	1
			Chase, et al. 2005	2
			Quist & Duray 2007	2
			Alcantara & Mayer 2008	0
3	Were inclusion / exclusion criteria specified?	The report described a list of criteria to determine eligibility for the study and a similar list for exclusion. The item was partially met if only inclusion or exclusion criteria were specified	Broide, et al. 2001	2
			Barber & Ring 2002	0
			Bishop et al. 2003	0
			Chase, et al. 2005	1
			Quist & Duray 2007	1
			Alcantara & Mayer 2008	0
4	Are the outcomes to be measured clearly stated?	The report describes the outcome measures to be used and how they are documented	Broide, et al. 2001	2
			Barber & Ring 2002	0
			Bishop et al. 2003	2
			Chase, et al. 2005	2
			Quist & Duray 2007	0
			Alcantara & Mayer 2008	0
5	Are the interventions clearly described?	The report describes the interventions. This item is partially met if only some aspects of the intervention are described, but not to the extent it is reproducible by another clinician	Broide, et al. 2001	1
			Barber & Ring 2002	2
			Bishop et al. 2003	0
			Chase, et al. 2005	2
			Quist & Duray 2007	2
			Alcantara & Mayer 2008	2

Table 2.2 (Cont) Scoring of six articles using the author's 7-point modified criteria

Number	Criterion	Satisfied if…	Reference	Score
6	Did the study provide point measures for at least one key outcome?	The report describes measures for at least one outcome before, at the end of intervention and at a further time period after the trial. The item is partially met if only two time points are described	Broide, et al. 2001	1
			Barber & Ring 2002	0
			Bishop et al. 2003	1
			Chase, et al. 2005	2
			Quist & Duray 2007	0
			Alcantara & Mayer 2008	2
7	Were there other factors that may affect outcome other than the intervention and was there adequate adjustment or acknowledgment of these confounders?	The report describes confounding factors that may have affected the outcomes of the study and acknowledges the effect they may have on the results. This item is partially met if only some of the main confounding factors are described.	Broide, et al. 2001	0
			Barber & Ring 2002	1
			Bishop et al. 2003	0
			Chase, et al. 2005	2
			Quist & Duray 2007	1
			Alcantara & Mayer 2008	2
	Total scores (out of 14)		Broide, et al. 2001	10
			Barber & Ring 2002	4
			Bishop et al. 2003	4
			Chase, et al. 2005	13
			Quist & Duray 2007	7
			Alcantara & Mayer 2008	7

Note. Yes = 2, partial = 1, no = 0.

The scores thus derived were aggregated and converted to a percentage of the maximum quality score of 14.

2.5 Results

The search strategy identified 468 articles. After screening the titles and abstracts of these articles 8 potentially relevant articles remained. Of these 2 were excluded as they were not in English (Sirenko, Chub, & Tsuketti, 1988; Weise, 1994). There were no randomised controlled trials and 6 remaining articles consisted of 3 case studies (Alcantara & Mayer, 2008; Barber & Ring, 2002; Quist & Duray, 2007),and 3 pre-post-intervention studies (Bishop, McKinnon, Weir, & Brown, 2003; Broide, et al., 2001; Chase, et al., 2005). The literature in this area is sparse.

As Table 2.2 demonstrates the study quality measured with the designed checklist ranged from 4 to 13 out of a possible 14 with a median score of 7. As the quality assessment questions already took into account that the methodological quality of the studies was not high, overall the resulting scores were poor. The quality assessment scores showed that the included studies described the interventions clearly. However, assessing disease status, stating study objectives and reporting inclusion and exclusion criteria were poorly done. Three studies did not state the outcome measures used (Alcantara & Mayer, 2008; Barber & Ring, 2002; Quist & Duray, 2007), and four studies did not report point measures for outcome measures, or only did so partially (Barber & Ring, 2002; Bishop, et al., 2003; Broide, et al., 2001; Quist & Duray, 2007). In all six studies the interventions were applied peripherally or externally to have an effect on a visceral organ. Characteristics of these studies are displayed in Table 2.3. Three of the studies were similar in that they were case studies reporting the effect of chiropractic treatment on a total of five children (Barber & Ring, 2002; Alcantara & Mayer, 2008; Quist & Duray, 2007). The intervention was spinal manipulation done for varying amounts of time ranging from one month to 15 months. Two of these three studies combined chiropractic treatment with either advice to cease the child's intake of wheat and dairy (Alcantara and Mayer), or abdominal massage (Quist and Duray). Three other studies investigated the effect of reflexology to the feet (Bishop, et al., 2003), acupuncture to points on the hand, foot and lower leg (Broide, et al., 2001) and transcutaneous electrical stimulation applied to the back and abdomen (Chase, et al., 2005).

Children who participated in these studies ranged in age from seven months to 16 years with 79% being male (this does represent the higher prevalence in boys as previously stated). Approximately 39% were ≤ 6 years. There were no adverse events reported in any of the studies. Broide et al. 2001 reported 10 children, and Bishop et al. 2003 reported 2 children dropped out of their respective studies, both early in the study and cited as due to lack of compliance in both instances.

All studies used subjective measures of bowel function as outcome measures; a bowel diary was kept by participants on a daily basis to record the frequency and ease of defaecation, stool consistency, episodes of faecal incontinence and abdominal pain (Alcantara & Mayer, 2008; Barber & Ring, 2002; Bishop, et al., 2003; Broide, et al., 2001; Chase, et al., 2005; Quist & Duray, 2007). Three of the six cited studies relied on parental verbal accounts rather than recordings made in a bowel diary (Alcantara & Mayer, 2008; Barber & Ring, 2002; Quist & Duray, 2007; Bishop, et al., 2003). Only one study (Broide, et al., 2001) used an objective measure of panopioid levels in venous blood before and after acupuncture. The outcome measures used in the six included studies therefore, were all based at the impairment level of the International Classification of Functioning. None of the studies investigated the effect of treatment on activity (for example, physical activity levels) or participation (for example quality of life, well-being, self-esteem, behavioural comorbidities). All studies indicated that using the subjective outcome measures the children benefited from the interventions.

Bishop et al. (2003) reported an improvement in frequency of bowel actions and reduction in soiling in children as a result of 6 weekly sessions of reflexology to the feet in a study completed by 48 children. Chase et al.(2005) reported similar improvements in improved defaecation frequency and reduced soiling as a result of electrical stimulation. The study reported by Broide et al.(2001) had a series of placebo treatments prior to real acupuncture treatment, and also a control group of children whose venous blood panopioid levels were compared to the treatment group at baseline and were found to be a significantly lower in the constipated children. Unfortunately this was not repeated in the control group 15 weeks later although it was reported to have increased significantly after treatment in the constipated group. The authors could not explain this, as a higher panopioid level would usually contribute to the symptoms of constipation. The treatment group had 5 placebo acupuncture sessions followed by 10 true sessions over a period of 15 weeks. There was a significant increase in bowel movements per week during and at the end of the real acupuncture sessions.

Table 2.3Summary of findings of the 6 articles included in this review

Table 3

Summary of findings of the 6 articles included in this review

Referenc e	**Score**	**Type of study**	**Participants**	**Interventions**	**Outcomes**
1. Broide et al. 2001	11	Crossover before and after intervention	17 (12 boys) mean age 6 years (3-13 yrs) 15 "controls" (10 boys) mean age 9 years (2-14 yrs) had baseline blood test only	5 weekly placebo acupuncture sessions, followed by 10 weekly real acupuncture session	Bowel diary of bowel actions/week Venous blood samples to measure plasma opioid level at baseline, 5, 10, 15 weeks of trial. "Controls" had similar blood levels done at baseline only
2. Barber et al. 2002	2	Case study	Female aged 6 years	Spinal manipulation 4 times in 10 weeks 5 months later, 5 times over 4 weeks 10 weeks later weekly for 4 months	Parent and child verbal report of faecal incontinence
3. Bishop et al. 2003	3	Before and after intervention	50 children aged 3-14 years. 64% boys, 18% girls. 30 children >6 years-old	Six 30-minute sessions of reflexology to feet at weekly intervals	Bowel diary reporting frequency of bowel actions and soiling at baseline, during and conclusion of study
4.Chase et al. 2005	13	Before and after intervention	8 children, 3 male, aged 7-16 years	20-30 mins of electrical stimulation applied over spine and abdominal wall 3/week for 9-12 weeks	Bowel diary for 1 month before, during and after intervention and for 2 weeks 3 months post intervention. Recorded bowel actions, soiling episodes, abdominal pain, medications, bowel washouts
5 .Quist et al. 2007	3	Case study	8 year old boy	Spinal manipulation and abdominal massage 2/week for 4 weeks	Parent report of bowel action frequency and abdominal pain.
6. Alcantara et al. 2008	5	3 case studies	Male aged 21 months	Spinal manipulation 1-3/week for 8 weeks	Parent reported descriptions of bowel function

2.6 Discussion

The literature identified in this review to establish the efficacy of non-pharmacological, non-surgical and non-behavioural treatments of functional chronic constipation in children is poor, and it appears by the papers found (2001 onwards) that interest in this area is relatively new.

The efficacy of chiropractic, reflexology, acupuncture or transcutaneous electrical stimulation has not been established by this review, however they have been identified as treatment modalities, and there is some preliminary evidence to suggest that they deserve further investigation. This is particularly so of acupuncture and transcutaneous electrical stimulation being the two highest scoring papers in the quality evaluation.

Children in three of the six studies (Alcantara & Mayer, 2008; Barber & Ring, 2002; Bishop, et al., 2003) were assessed incompletely for their bowel dysfunction, therefore it was not established if the children's symptoms were transitory (therefore likely to resolve with time) or chronic. In the three studies which did assess constipation according to accepted definitions (Broide, et al., 2001; Chase, et al., 2005; Quist & Duray, 2007) the children had longer duration symptoms and therefore were likely to be more difficult to treat. This is particularly so in the studies by Broide, et al., 2001 and Chase, et al.(2005) where the children had not responded to former treatments and had more severe symptoms. This adds weight to the comment that these interventions deserve more study.

Outcome measures in infants are difficult to assess, as bowel function is so variable depending on type of feeding, levels of hydration and amount and type of food ingested and food sensitivities for example. Symptoms that resolve within several weeks may have done so anyway. One study treated a 21- and 7-month-old and the reported improvement was still at the very lower level of normal frequency for defaecation for infants of that age (Alcantara & Mayer, 2008). In the same paper a 21-month old girl who had constipation since having cow's milk introduced at 10 months of age suffered pain and rectal bleeding, characteristics of milk protein intolerance. Any dietary measures taken were not reported as they were in the previous case.

Only one paper discussed the issue of a placebo response or change in the child's behaviour as a result of attending a caring health professional regarding a sensitive issue over a period of time (Chase, et al., 2005). Broide et al (2001) noted a significant increase in defaecation frequency in female participants during the placebo acupuncture sessions, clearly demonstrating this confounding effect. Infants in the studies may not be influenced by a placebo response, but one can argue that the parent or carer may be influenced, which in turn has an effect on the child.

Other confounding effects decreased the quality of these studies, for example, implementing two interventions concurrently – diet change (Alcantara & Mayer, 2008) or abdominal massage (Quist & Duray, 2007) with spinal manipulation, or eliminating a treatment concurrently (Bishop, et al., 2003). Bishop et al. ceased carrying out enemas on the children when reflexology began, and noted that as a result, parents were less anxious, family relationships less strained and treatments were less traumatic for both children and nurses. As one of the precipitating and perpetuating causes of constipation in children is anal or rectal pain or discomfort, or fear of these; this is a confounding factor in this study.

The mode of action or physiological response for each of these treatment modalities can only be postulated. It has been suggested that the autonomic nervous system is either facilitated (via parasympathetic nerves) or inhibited (via sympathetic nerves) by manipulation, acupuncture or electrical stimulation. Electrical stimulation has the potential to either directly stimulate the enteric (intrinsic) nerves of the large bowel, or the extrinsic nerves (vagus, hypogastric or sacral). Acupuncture has been shown to accelerate the release of neurotransmitters (eg. opioid peptides) in the central nervous system. Each of the interventions studied has the potential to cause a reflex action through somato-visceral reflexes via peripheral sensory stimulation. Further research is needed to elucidate the neurophysiological effects of these interventions on visceral organs.

2.7 Conclusion

This review has shown that the literature in the area of interest is sparse and the evidence for the efficacy of the interventions identified of low quality, at best Level IV National Health and Medical Research Council (National Health and Medical Research Council. 2008 – 2009). In view of the great need for new effective treatments for chronic constipation in children, and that this preliminary evidence showed some benefit, further research should to be undertaken into the interventions identified. There is a need for randomised controlled trials involving participants who have been diagnosed and classified according to the currently accepted definitions of childhood constipation. Well-defined inclusions and exclusion criteria and objective outcome measures, such as bowel transit studies, need to be used as well as bowel diaries. Validated quality of life and behavioural questionnaires will give more information about the wellbeing of the child before and after intervention. Longer follow-up is required to further clarify effect and identify placebo response.

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CHAPTER 3: PREFACE

Chapter 3 presents a randomised controlled trial investigating the use of interferential current to treat Slow Transit Constipation in children. It has been submitted for publication to Gastroenterology. The format has been changed to be consistent with this thesis and tables and figures have been inserted for ease of reading.

CHAPTER 3: TRANSCUTANEOUS ELECTRICAL STIMULATION TO TREAT CHILDHOOD SLOW TRANSIT CONSTIPATION: A RANDOMISED SHAM-CONTROLLED TRIAL

3.1 Abstract

Background and Aims

Slow-Transit Constipation (STC) in children is characterised by slow transit along the entire colon diagnosed by bowel transit studies. Infrequent bowel actions, faecal incontinence and abdominal pain are often refractory to medical management. Following a pilot study applying transcutaneous interferential current (IFC) in children with STC, we undertook a randomised controlled trial to determine whether IFC was effective in controlled conditions.

Methods

Forty-six children (28 boys, 18 girls, 8 -18 years) with STC were recruited. Children's bowel symptoms and quality of life (QoL) (PedsQL) were assessed initially, after a 4-week baseline period and 8 weeks post-intervention. Children were randomly assigned to twelve 20-minute sessions over 4 weeks of real or sham stimulation. Trained physiotherapists applied stimulation via 4 self-adhesive electrodes, 2 paraspinally and 2 over the abdomen. Current at a comfortable intensity was applied with a varying beat frequency of 80 to 150Hz. Number of defaecations, episodes of soiling, pain and laxative use were recorded in daily diaries. Colonic transit using scintigraphic geometric centres of activity at 6, 24, 30 and 48 hours were compared pre- and 6-8 weeks post-treatment (paired t-test).

Results

There were no differences in the groups pre-treatment. Active stimulation vs sham resulted in i) faster colonic transit times p=0.007) ii) decreased number of days with abdominal pain (p=0.0002) and soiling (p=0.002), and iii) improved self-perceived physical QoL (p=0.01).

Conclusion

Transcutaneous IFC improved colonic transit and physical QoL and decreased faecal incontinence and pain in children with STC.

3.2 Introduction

Childhood constipation is common with 5-10% of paediatric outpatient appointments being associated with constipation and/or faecal incontinence. The majority of children respond to pharmacological therapy and behavioural modification programmes. Despite these interventions one third of children carry the condition into adulthood (van Ginkel, Reitsma, van Wijk, Taminiau, & Benninga, 2003).

Slow-transit constipation (STC) is a condition of colonic dysmotility diagnosed by nuclear or sitz marker transit studies with slow transit of contents along the proximal colon (Benninga, et al., 1996; Gutierrez, Marco, Nogales, & Tebar, 2002; Hutson, et al., 2004). The cause of STC is not known. Hypotheses range from primary (or developmental) dysfunction to hormonal disorders. It is possible there is a genetic link, with 5%-10% of families having more than one member affected (Hutson, McNamara, Gibb, & Shin, 2001). Dysfunctional enteric nervous system, decreased levels of substance P, decreased numbers of Interstitial cells of Cajal and connective tissue disorders have all been implicated (Hutson, et al., 2004; Meier-Ruge, Holschneider, & Scharli, 2001)

Resultant soiling, recurrent faecal impaction and abdominal pain have significant social and emotional consequences for the child and family. Children with STC have been shown to have an impaired quality of life (Clarke, et al., 2008).

Transcutaneous electrical stimulation using interferential current (IFC) has previously been used for pain management (Robertson, Low, Reed, & Ward, 2006) and treatment of urinary incontinence (Laycock & Green, 1993). IFC involves the use of slightly out-of-phase alternating electrical currents arranged to produce a current within the tissue (Robertson, et al., 2006). Diarrhoea has been reported as a side effect (Emmerson, 1987). In a pilot study of children with chronic constipation IFC increased defaecation frequency in 5 out of 8 children (Chase, Robertson, Southwell, Hutson, & Gibb, 2005).

The aim of the present randomised study was to determine whether IFC improved colonic activity and defaecation in children with STC. We hypothesised that a randomised controlled trial would show that colonic transit time, defaecation frequency, faecal incontinence, abdominal pain and quality of life would be improved by active compared to sham electrical stimulation.

3.3 Methods

Forty-six children with STC (28 boys, 18 girls, aged 8-18 years) were recruited from the Continence, Surgical and Gastroenterology outpatient clinics at the Royal Children's Hospital, Melbourne. Ethics approval had been given by the Royal Children's Hospital Ethics in Human Research Committee (EHRC 23040A). (see Appendix B)

3.3.1 Trial Design

The randomised study comprised 4, four-week intervals: – i) 1 month baseline, ii) 1 month of active or sham stimulation, iii) 1st month post-treatment and iv) 2nd month post-treatment (figure 3.1). These follow-up periods were based on the observation that children in the pilot study had long-lasting effects for at least two months after treatment. The mean number of defaecation episodes, soiling and abdominal pain each week were calculated for each interval and compared before and after treatment (active and sham). Quality of life (PedsQL) and colonic transit were measured before and after the treatments. (see Appendix C & D)

3.3.2 Clinical Assessment

Initial assessment of each child by the paediatrician (SG) and continence physiotherapist (JC) included bowel dysfunction (history, past medical management, neonatal/developmental issues, present bowel and bladder symptoms and management), routine measurements of weight, height, blood pressure and pulse rate (lying and standing) and assessment of faecal loading by abdominal palpation. After 4 weeks of baseline recording, faecal loading was again assessed by abdominal palpation. (Figure 3.1) Children with palpable faecal masses were prescribed macrogol 3350 for 3 days prior to commencing IFC. Maintenance laxative treatment was continued throughout the treatment and follow up periods. If necessary, doses were adjusted by the paediatrician. No subjects had their laxative dosage increased during treatment or follow up.

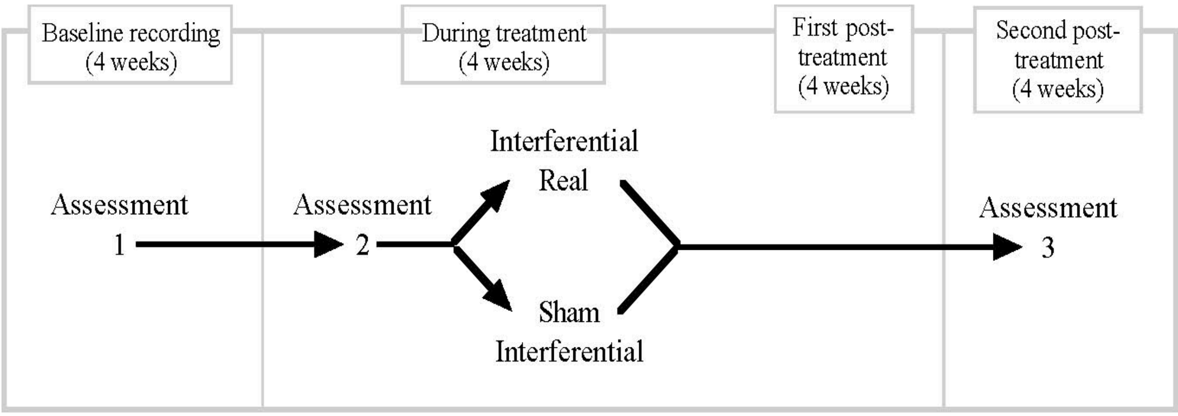

Figure 3.1 Trial design

3.3.3 Inclusion criteria

All children had more than two years chronic constipation as defined by Rome III criteria (Benninga, et al., 2005) which had not responded to standard therapies (diet, laxatives, behavioural modification therapy) or were laxative dependent. They were all screened to exclude Hirschsprung's disease, coeliac disease, hypothyroidism or allergies, which may impact on bowel function. STC was diagnosed by radionuclear transit studies (Cook, et al., 2005) within the prior year. STC was defined by retention of radioisotope in the ascending, transverse, and descending colon 48 hours (Gutierrez, et al., 2002).

3.3.4 Exclusion criteria

Children were excluded if they had had bowel surgery other than the formation of an appendix stoma for antegrade colonic enemas (King, Sutcliffe, Southwell, Chait, & Hutson, 2005), or if they had any contraindication to the application of electrical current (diminished skin sensation, risk of skin irritation, cardiac pacemaker), or had previously had electrical stimulation for any condition. Children with neurological disorders or children and their families with conditions that did not allow them to complete the questionnaires or bowel diaries were also excluded.

3.3.5 Active or sham stimulation

Treating physiotherapists (n = 26) were recruited from clinics close to the home of each participating child and provided with two identical IFC machines (Vectorsurge 5 VS470, Metron Medical, Carrum Downs, Victoria, Australia) labelled underneath A or B. Machine B (sham IFC) was altered by the factory so it delivered no current but the usual output lights and dials indicated changing intensity levels matching the other machine.

Machines delivered two channels of alternating current. One channel had a fixed frequency of 4 kHz, but the other varied from 4080 to 4150Hz, producing a varying beat frequency of 80 to 150 Hz. The current (less than 40mA) was applied via two pairs (four) 50 x 50 mm self-adhesive conducting electrodes (Verity Medical Ltd, Hampshire, England). Two electrodes (one from each pair) were placed paraspinally from T9-10 to L2. The other electrode from each pair was positioned diagonally opposite on the anterior abdominal wall below the costal margin (Chase, et al., 2005). Current was applied for twenty minutes at barely sensory levels and sub-motor intensity so each child was aware of no more than low to medium sensory stimulation and no abdominal wall muscle contractions occurred. IFC stimulation was given three times per week for four weeks. This treatment protocol was based on the recommendations of de Domenico (1987) who published the only previous work on using IFC for STC.

3.3.6 Randomisation

Instructions to administer either active or sham stimulation were randomised in blocks of 6 and sealed into numbered envelopes. When a child was recruited, the next envelope was mailed to the treating physiotherapist. The treating physiotherapist ensured the trial physiotherapist remained blinded to its contents. On completion of one month of stimulation, the treating physiotherapists mailed the treatment record to the trial office. The code was broken after data entry and analysis.

3.3.7 Blinding

Patients and all trial staff except for the treating physiotherapist were blinded to treatment. Because all machines were connected to 240 V power, for safety reasons the treating physiotherapists could not be blinded to the treatment. Physiotherapists were given a written script and trained to present the stimulations in exactly the same way with both machines and to offer no other advice or intervention. This helped to ensure that patients received identical treatment with each machine.

3.3.8 Outcome measures

Primary outcomes were defaecation and soiling measured by daily diaries. (see Appendix E) Secondary outcomes were colonic transit rate (using a radionuclear transit study) and quality of life measured by questionnaire.

3.3.9 Nuclear transit studies

All children had a radio-nuclear colonic transit study prior to entering the trial (Cook, et al., 2005). Children drank a radioactive drink and had gamma camera images taken at 0,2,4,6, 24, 30 and 48 hours. The geometric centre of radioactivity was calculated (Cook, et al., 2005). As the pilot study suggested the effect of electrical stimulation lasted at least two months, the second transit study was performed eight weeks after the end of the four weeks of active or sham stimulation. The geometric centres of radioactivity for the active and sham groups were compared before and after electrical stimulation by a blinded assessor.

3.3.10 Daily diaries

A daily bowel diary, completed through 16 weeks of the trial, recorded seven items -

1) Whether a bowel action occurred during a timed sit on the toilet or was spontaneous (going to the toilet in response to an urge to defaecate).
2) Stool consistency, using the Bristol Stool Scale (Riegler & Esposito, 2001),
3) Soiling episodes.
4) Laxatives or bowel washouts (name, dosage).
5) Abdominal pain.
6) If electrical stimulation was given.
7) Any mitigating circumstances such as intercurrent illness.

3.3.11 Quality-of-Life Measures

Quality of life was measured using Paediatric Quality of Life Inventory (PedsQL).(see Appendix C & D) This was administered to both parent and child after the baseline month and again 2 months after the end of the course of stimulation (Figure 3.1). The PedsQL 4.0 Generic Core Scales consist of parallel parent and child self-report scales and have been validated in children and adolescents aged 2 to 18 years (Varni & Kurtin, 2001; Varni, Seid, & Rode, 1999; Varni, Seid, Knight, Uzark, & Szer, 2002). The questionnaires consist of 23 items encompassing (i) physical (8 items); (ii) emotional (5 items); (iii) social (5 items); and (iv) school (5 items) functional domains. The categories can then be grouped into physical (i) and psychosocial (ii, iii, and iv) areas. The questions ask how much of a problem each item has been during the past 1 month. A 5-point response scale is used (0 =never a problem; 1 = almost never a problem; 2 = sometimes a problem; 3 = often a problem; 4 = almost always a problem). Items are reverse-scored (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0) and linearly transformed to a 0 to 100 scale. Higher scores indicate better quality of life.

Each parent and child completed the questionnaires independently with impartial assistance being provided for any child who had difficulty with comprehension.

3.3.12 Sample size

During the pilot study, 5 out of 8 (62.5%) children increased the frequency of defaecation episodes into the normal range. Based on this study it was expected that the placebo effect would be between 30-40%. An initial power analysis concluded that with a sample size of 60 this study would show a statistically significant change if improvement with treatment was 25% better than the improvement with sham. Interim analysis of transit, soiling and quality of life was done on 35 children (18 sham and 17 active treatment). Active treatment was found to produce a statistically significant benefit compared to sham treatment. At this point a further 11 children who had already enrolled in the trial completed the protocol, but no further participants were recruited.

3.3.13 Statistics and data analysis.

Paired t-tests were used for analysis of parametric data obtained from particpants before and after the course of stimulation. Defaecation, soiling and abdominal pain were analysed in 4 intervals. This monthly data was compared by one-way ANOVA with Tukey’s post-test to determine if any groups were significantly different from one another. All p values <0.05 were considered as statistically significant. Between group comparisons of the efficacy of treatment were not conducted because children were not stratified for the severity of their soiling, spontaneous versus timed defaecations and by management strategies.

3.4 Results

Between February 2006 and November 2008, 46 children commenced the trial, and 42 (24 boys, 18 girls) completed it. Four male participants were excluded; two lost bowel diaries and two broke study protocol. Twenty-one children (12 male) had active and 21 (12 male) had sham treatments. No adverse events were reported in this study.

During the baseline period, before treatment commenced, there were no significant differences between the active and sham groups in gender, age, episodes of abdominal pain, frequency of defaecation or episodes of faecal incontinence or quality of life (Table 3.1)

Diary Item	**Sham Stimulation**	**Active Stimulation**	***p***
Number of children	21	21	
Male : Female ratio	1.3 : 1.0	1.3 : 1.0	
Age in years, mean (range)	11.6 (7.8 – 16.5)	11.3 (7.4 – 17.7)	
Mean Age of Male / Female (years)	11.2 / 12.0	11.8 / 10.6	
BMI			
Underweight (<5th percentile)	0 / 21	1/21	
Healthy (5-85 percentile)	16 / 21	16 / 21	
Overweight (85-95 percentile)	4/21	2/21	
Obese (>95th percentile)	1/21	2/21	
Duration of symptoms: Mean (range) years	8.7 (2.7 – 14.4)	9.7 (4.4 – 13.9)	
Had symptoms since birth	4/21	7/21	
Defaecation episodes/week, mean (range) [1]	5.23 (1-13.25)	6.46 (0-21)	0.39
Ongoing treatment			
Taking medication (laxatives)	18 / 21	16 / 21	
Appendix stoma (for antegrade enemas)	2/21	3/21	
Faecal incontinence (soiling)			
No soiling	2/21	5/21	
Moderate soiling (<2 episodes/wk)	5 / 21	3 / 21	
Severe soiling (≥2 episodes/wk)	14 / 21	13/21	
Incontinence episodes/wk, mean (range)	2.79 (0-6.5)	3.06 (0-7.0)	0.7
Pain			
Have abdominal pain	15 / 21	17 / 21	
Number of days with pain/wk, mean (range)	1.98 (0-6.5)	2.01 (0-5.5)	0.95
Mean pain score (0= low, 10=high)	5.5	4.5	

Table 3.1 Pre-treatment demographics of children in sham and active stimulation groups showing diary data.

Data is shown as mean (range). P values are for t tests comparing sham and active groups for the factor in the row. [1] Number of defaecations per week is for patient with ongoing laxative treatment. Patients are still constipated with this treatment and number of defaecations is not effective to empty the colon.

3.4.1 Colonic transit

Before stimulation, colonic transit was similar in the active and sham groups (Figure 3.2). The transit study was able to be repeated 8 weeks after stimulation in 30 of the 42 children (Figure 3.2) Eight weeks after stimulation, colonic transit was significantly more rapid in the children who had received active stimulation. Transit was faster at 24 hours (p=0.001), 30 hours (p=0.038), and 48 hours (p=0.007) after ingestion of radiolabel (Figure 3.2). There was no significant difference in colonic transit in those children who received sham stimulation.

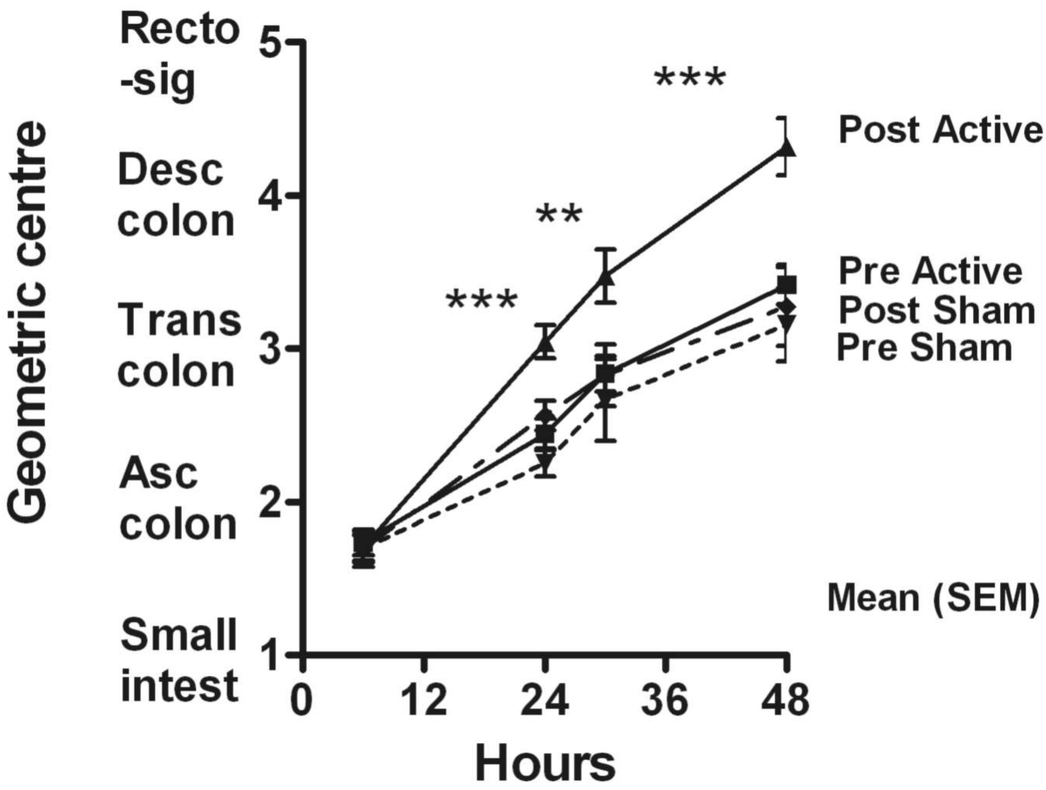

Figure 3.2 Transit data.

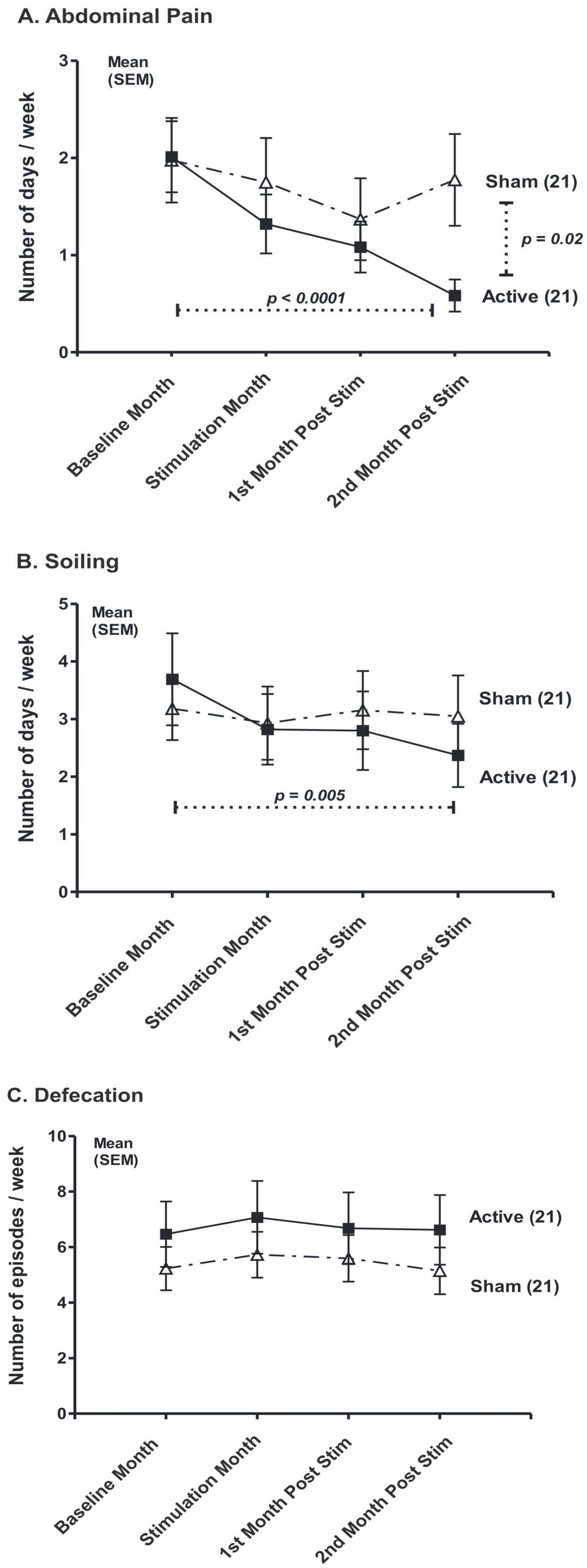

Figure 3.3 Results
– A. abdominal pain B. soiling & C. defaecation

3.4.2 Abdominal Pain

Following active treatment, there was a significant decrease in the number of days with abdominal pain each week compared to baseline during the first (p = 0.02) and second (p = 0.0002) post-treatment months (Figure 3.3 A). There was also a reduction in the number of days with abdominal pain each week in the sham group during the first month after treatment (p=0.02), but not during the second post-treatment month (p = 0.48).

3.4.3 Faecal incontinence

There was a significant decrease in the number of episodes of soiling each week in the group of children who received active treatment (Figure 3.3 B) in the 8 weeks after treatment (p = 0.002) compared to baseline, but not in those who received sham treatment (p = 0.68).

3.4.4 Defaecation

There was no significant change in the number of defaecations during timed sits or spontaneous defaecations each week in either active or sham treated groups during the first and second post-treatment months compared to baseline (p = 0.88 active, p = 0.85 sham, Figure 3.3 C)

3.4.5 Quality-of-Life

The children's self-perceived overall PEDsQL score was significantly improved in those who received active treatment but not in those who received sham treatment. Children who received active treatment had a significant improvement in the physical domain of their quality of life scores (Table 3.2). Sham-treated children had no significant change in physical score.

Parents perceived no significant change in the quality of life of their children after either active or sham stimulation. Overall and subscale measures of parental-reported PEDsQL showed no significant improvement after either active or sham stimulation.

Measure	Intervention	Before intervention	After intervention	*p*
PEDsQL Score as perceived by child				
Physical score	Sham	84.0	84.9	0.21
	Active	77.6	84.2	**0.02**
Psychosocial score	Sham	68.2	73.8	0.23
	Active	72.0	78.6	0.15
Total score	Sham	72.2	76.6	0.22
	Active	73.4	80	**0.06**
PEDsQL Score as perceived by parents…				
Physical score	Sham	82.5	82.5	1.0
	Active	74.8	71.7	0.54
Psychosocial score	Sham	65.9	68.1	0.66
	Active	62.8	65.1	0.77
Total score	Sham	70.1	71.7	0.70
	Active	66	68.3	0.69

Table 3.2 Results Quality of Life (QoL)

3.5 Discussion

The results show 12 treatments of IFC, applied over 4 weeks, significantly improved symptoms in children with STC. Real IFC produced significantly decreased colonic transit time, fewer days with abdominal pain and faecal incontinence and, increased self-perceived physical quality of life. Sham IFC did not. The finding in this study of decreased colonic transit time as measured by nuclear transit studies is particularly encouraging as we have already established such studies to be an effective and reproducible means of assessing slow colonic transit in children, and therefore can be reliably used to assess response to treatment.

No previous studies have used electrical current to treat this condition in children. However, studies in adults have implanted sacral nerve stimulation with encouraging results (Dinning, Fuentealba, Kennedy, Lubowski, & Cook, 2007; Mowatt, Glazener, & Jarrett, 2008). This method has been used for combined bowel and bladder dysfunction in children with reported improved defaecation rates (Humphreys, et al., 2006; Roth, Vandersteen, Hollatz, Inman, & Reinberg, 2008). This approach is invasive, and reported adverse events are infection, electrode migration and the need for lead revision.

The rationale for this selection of parameters was based on several things. De Domenico describes the use of IFC to treat constipation using the same parameters and electrode placement (De Domenico, 1987). No evidence is given. However a study done using IFC with similar electrode placement to treat overactive bladder in patients with Multiple Sclerosis, reported the side effect of diarrhoea, implying an effect of bowel motility (Emmerson, 1987). In the absence of other protocols, and as neither author had reported adverse effects, this became the protocol for the pilot study and randomised sham-controlled trial. These treatment parameters may not be optimal and further research is needed to investigate optimum frequency of current, frequency and duration of treatment and electrode placement.

Children with STC can be challenging to treat. Laxative and toileting programs are the usual treatment approaches but often have limited success. Children in this study had not responded to these interventions and their transit times and symptoms had not changed. Typically, the child and family are left with all the physical, emotional and financial consequences of a chronic medical condition (Clarke, et al., 2008).

Quality of life in children with STC is comparable to those with cancer or cystic fibrosis (Clarke, et al., 2008). Children with faecal incontinence are reported to have more behavioural comorbidities which can further affect compliance with treatment (Benninga, Voskuijl, Akkerhuis, Taminiau, & Büller, 2004). Bower (2008) reported that boys in particular who soil, and have treatment which has failed to improve their condition, have a lower quality of life. If carried into adulthood, constipation is a risk factor for urinary incontinence in women (Chiarelli, Brown, & McElduff, 1999), and pelvic organ prolapse (Hunskaar, et al., 2005).

This study revealed that child-perceived physical quality of life improved in children who had real IFC. This may be associated with the improvement in bowel motility, and the decrease in abdominal pain and soiling this group experienced. We note that the group receiving sham stimulation did have a temporary improvement in abdominal pain but this was not sustained as it was in the real stimulation group, and may have been a placebo response. Both treatment groups showed significant differences in self-perceived total and psychosocial quality of life. We attribute this to the children feeling well-supported during the trial, and perhaps more hopeful as their condition was being researched and a new treatment was being sought. Parents of children in both groups did not report significant changes in quality of life. For those whose children had sham treatment and no lasting significant improvements in their symptoms, this is not surprising. We propose that parents of children in the real treatment group also felt their children had no difference in quality of life, as it would take more than a few months before they could be certain that the years of difficulties were behind them.

There are particular problems in conducting a RCT which involves applying electrical stimulation. First, for safety and practical reasons, the physiotherapist applying the treatment cannot be blinded to the treatment. Patient reports of sensation typically indicate a level of output current. Participating physiotherapists were trained how to administer the treatment, what to say and to not enter into discussion about results. They were instructed to behave in an identical manner for all applications, returning apparently to increase the intensity level of current during treatment with both sham and real machines. Children were told they may or may not feel something, but to report any tingling. Some children reported tingling when the sham machine was applied and no child in the study intimated they were aware which machine was used to treat them.

Second, there was no sensation of current with applications using the sham machine. To avert participant awareness that this might mean they were in the sham group, different methods of applying the current were considered. IFC can be applied via self-adhesive skin electrodes or electrodes held on using suction cups. We decided against using suction electrodes as the possible contribution of their effects on sensory pathways is unknown. Similarly, we decided not to use heating as the sham treatment but to use the same electrodes and equipment and ensure consistent instructions and advice by the treating therapists.

One possible explanation of the outcome is that visiting a caring health professional on a regular basis could have a positive behavioural training effect. However the treating physiotherapists were trained to apply the treatment and not discuss or advise in any other way. All participants and their parents had received considerable medical and behavioural input previously and this had not affected their bowel motility. Finally, there were no significant improvements in the sham group, confirming that the relationship with the physiotherapist did not affect the outcome.

Our results show that electrical stimulation influenced bowel motility by this treatment, but the mechanism of the effect is, at present, unknown. Larger diameter nerves will selectively be stimulated before smaller diameter nerves. The intensity of stimulation was comfortable; so we assumed we did not stimulate A-δ or C-fibres, but more likely superficial A-α and A-β fibres. The importance of the location of the electrodes is also unknown. Although IFC is traditionally accepted as having a particular pattern of distribution this has shown not to be so (Robertson, et al., 2006). Modulated IFC applied to the trunk will spread in many directions according to the tissue arrangement because of differences in their impedance, and unless the orientation of nerve fibres is optimal stimulus modulation may be partial (Ward, 2009).

Neuromodulation of the bladder with electrical current is a well-established treatment in adults and children. This possibly acts centrally by re-balancing excitatory and inhibitory information and returning the neural drive towards a more normal status. In the treatment of detrusor over-activity this is done less invasively with transcutaneous electrodes (Hoebeke, Renson, Petillon, Vande Walle, & de Paepe, 2002). Gooneratne et al. (2008) demonstrated changes in levels of substance P in the rectal mucosa following both 14 and 90 days of continuous sacral nerve stimulation giving objective evidence of change that occurs with neuromodulation.

The effect might be due to direct stimulation of the enteric nerves or pacemaker cells. Stimulation of extrinsic nerves, an excitatory effect on sacral or vagal nerve fibres, or an inhibitory effect on thoracolumbar sympathetic nerves, is possible. Another option is a reflex effect via somatovisceral reflex activity explained by reciprocal depolarisation of visceral and somatic afferents converging on lamina 5 of the dorsal horn of the spinal cord, resulting in central relay of information (Camilleri, Malageladam, Kao, & Zimnmeister, 1984).

Neuromodulation of the bowel provides a reasonable explanation for the effect in the participants as a bowel action was rarely stimulated by treatment immediately. Rather, we noted a more gradual improvement over successive days and weeks. Another explanation might be that there were trophic effects in the bowel as a result of the application of current, which led to improved bowel functioning.

Although there was a significant decrease in bowel transit time, pain and soiling, the number of defaecations did not change to the same degree. One explanation may be that it takes some months for the children to learn to adapt to, and interpret the new sensations they feel as a result of treatment, before the number of spontaneous defaecations increases. The improvement in the sensation of the need to defaecate was notable, some children commenting that they had never felt it before. We did not measure stool volume. As soiling decreased, it is conceivable that although frequency of defaecation did not increase, efficiency of bowel evacuation did. Real treatment was found to produce statistically significant improvement in soiling compared to sham treatment. When a battery operated machine became available, children who had completed this trial with little effect took the battery machine home and did daily stimulation. Defaecation increased in 9/11 children using home stimulation suggesting that more frequent stimulation is more effective in increasing defaecation (Ismail, et al., 2009).

Many of the children took high levels of laxatives and had 4 timed sits on the toilet each day. They passed small volumes during these sits. As the diaries recorded number of defaecations and not volume, these appeared as many defaecations/week, and gave a false impression of the children not complying to the expectation of <3 defaecations/week accepted in the Rome criteria.

For this reason we chose not to compare the two groups based on the outcome measure of defaecation frequency. Future work should consider the problem of standardising symptoms at baseline and may involve the development of a summed score for dysfunction that includes all of the symptoms of interest (e.g. number of spontaneously passed stools, number of prompted stools, stool volume, soiling by severity, duration and or frequency of abdominal pain). Such a score would facilitate between group comparison of the efficacy of IFC when compared to sham or placebo treatment.

3.6 Conclusion

Transcutaneous electrical stimulation using IFC increased bowel motility, decreased bowel transit time, pain and soiling and improved physical quality of life in children with STC. More research is needed to determine optimum stimulation parameters including electrode position, parameters of current, frequency and duration of treatment.

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CHAPTER 4: TRANSCUTANEOUS ELECTRICAL STIMULATION TO TREAT CHILDHOOD SLOW TRANSIT CONSTIPATION USING TENS AND PORTABLE INTERFERENTIAL – A PILOT STUDY

4.1 Introduction

In the randomised controlled trial reported in Chapter 3, children with slow transit constipation (STC) were treated at a physiotherapy practice with interferential current (IFC) three times per week. Participant safety was ensured by having a registered physiotherapist operate the IFC machine and by using clinical premises that were electrically wired according to specific safety regulations for interferential machines powered by mains current. Visiting a physiotherapy practice three times per week was time-consuming for families and only available to children who lived within reasonable distance of a practice. The feasibility of IFC treatment for other children who, for example, lived in rural areas was limited. For children who could not access a public health facility, because of lack of proximity, but could attend a private physiotherapy practice, this option could be limited because of financial constraints.

After commencing the randomised controlled trial, a new portable battery-operated interferential machine became available in Australia (EPM IF 4160-AltoHealth Pty Ltd). Once the trial period was completed, children who had not responded to treatment three times weekly were offered daily electrical stimulation treatment at home with the portable machine. Defaecation frequency improved with this treatment (Ismail, et al., 2009), and this group of parents and children coped well with applying IFC, having had previous experience of receiving it from a physiotherapist. This provided evidence that home-based treatment was worth pursuing. However these portable IFC machines are quite expensive at $350.00 to $400.00 AUD per machine.

Transcutaneous electrical nerve stimulation (TENS) machines are designed for home use and are small, portable, battery-operated units. They are most commonly used by physiotherapists for pain management (analgesia). They deliver up to 80mAmp current intensity with cycles up to 150Hz frequency and varying pulse width, can be used for transcutaneous electrical stimulation and potentially provide an alternative to portable IFC. TENS units are relatively cheap to purchase –costing approximately $85.00 AUD.

As both TENS and IFC can deliver transcutaneous electrical stimulation it was of interest to assess if TENS could be used to treat children with STC at home as effectively as portable IFC. Although TENS units are not able sweep across a variety of frequencies as IFC units do, it is possible to choose a similar pulse width and represent the range of frequencies of interferential current by one frequency. If a similar result could be achieved with TENS this would mean a cheaper treatment option was available to families.

The first question to be answered was, was it feasible to train and have parents perform transcutaneous electrical stimulation at home using TENS or IFC, not having had any experience of this mode of treatment previously? The second question was did TENS have a comparable effect to IFC on bowel dysfunction?

The aim of this pilot trial was determine if daily electrical stimulation in the form of either TENS or portable, home based interferential current (IFC) could improve the symptoms of slow transit constipation (STC) in children. Permission for this trial was granted by HREC at Royal Children's Hospital (No 26173A) (see Appendix F)

4.2 Method

4.2.1 Study design

The study ran over a period of 20 consecutive weeks, divided into 4 weeks pre-treatment phase, an 8 week treatment phase and an 8 week post-treatment phase (see Table 4.1).

TIME	*LOCATION*	*PURPOSE*
Week 0: Contact 1	*Hospital visit*	*Initial assessment*
Weeks 1-4: pre-treatment phase	*Home*	*Baseline bowel diary completion*
End week 4:Contact 2	*Hospital visit*	*Randomisation to receive either TENS or IFC stimulation. Training in mode of stimulation allocated*
Weeks 5-8:treatment phase	*Home*	*Daily stimulation*
End of week 8:Contact 3	*Hospital visit*	*Assessment of progress*
Weeks 9-12: treatment phase	*Home*	*Daily stimulation*
End of week 12: Contact 4	*Hospital visit*	*Assessment of progress*
Weeks 13-20: post treatment phase	*Home*	*Follow-up period (with continuation of completion of bowel diary but no electrical stimulation)*
End of week 20: Contact 5	*Hospital visit*	*Repeat of initial assessment*

Table 4.1 Time-frame and study procedures

4.2.2 Participants

From a cohort of children with slow transit constipation attending outpatient clinics at the Royal Children's Hospital, Melbourne, eleven consecutive children who were referred between May and November 2008 and met the inclusion criteria were recruited for this study. All children had a nuclear transit study to confirm their initial diagnosis prior to the study.

Written informed consent was obtained from one parent of each participant, and verbal consent was obtained from every participant.

4.2.3 Inclusion/exclusion criteria

Inclusion criteria for the pilot trial were children aged between 4-18 years with more than two years of unsuccessfully treated bowel dysfunction and soiling and 6 months of documented treatment (such as diagnostic tests, laxative use, and toileting programmes).

Exclusion criteria were any contraindications to transcutaneous electrical stimulation for example, diminished skin sensation, a risk of skin irritation, or the presence of a pacemaker. In addition any condition that affected the ability of the child or family to safely implement the treatment at home was an exclusion criterion, for example, a child unable to co-operate with quiet activities for a period of time during electrical stimulation application. An inability of parents or child to report and document bowel habits was also an exclusion criteria as this was the primary outcome measurement. Children with STC who had previous bowel surgery, or any child who had Hirschprung's disease, Coeliac disease or a metabolic disorder (for example, hypothyroidism) that caused constipation were excluded.

4.2.4 Outcome measures

Two outcome measures were used: a daily bowel diary and quality of life questionnaire. A daily bowel diary was introduced during the initial visit. (see Appendix G) All families were instructed in how to use it by either the assessing paediatrician or physiotherapist and asked to complete it daily for the twenty weeks. The bowel diary recorded seven items: (1) whether a bowel action was intentional (defined as occurring when the child tried to defaecate), or spontaneous (defined as a response to an urge to defaecate), (2) stool consistency, using the Bristol Stool Scale (Riegler & Esposito, 2001), (3) whether soiling occurred and if so, if it was a 'stain' (defined as underwear being able to be put straight into water to soak/wash) or 'scrape' (defined as solid material needing to be removed before underwear could be soaked/washed), (4) use of any laxatives or bowel washouts (name, dosage), (5) episodes of abdominal pain, (6) documentation of each electrical stimulation treatment session including the level of intensity of stimulation and (7) any mitigating circumstances such as intercurrent illness.

Parents and children in the trial were familiar with keeping bowel diaries as this is an integral part of management of STC. Fifteen minutes was spent ensuring that details of the diary were understood and written instructions were given (see Appendix G). It depended on the age and capability of the child as to whether the diary was completed by the child with supervision, or by the parents. At contact visits each page of the diary was scrutinised so that any ambiguity could be addressed with the parents and child.

Quality of life was measured using Pediatric Quality of Life Inventory (PedsQL). (see Appendix C & D) This was administered to both parent and child at the end of week 4 and again at week 20. The PedsQL 4.0 Generic Core Scales consist of parallel parent and child self-report scales consisting of 23 items encompassing (i) physical (8 items); (ii) emotional (5 items); (iii) social (5 items); and (iv) school (5 items) functional domains. For further details see Chapter 3, Methods, page 69.

4.2.5 Assessment

Initial Assessment

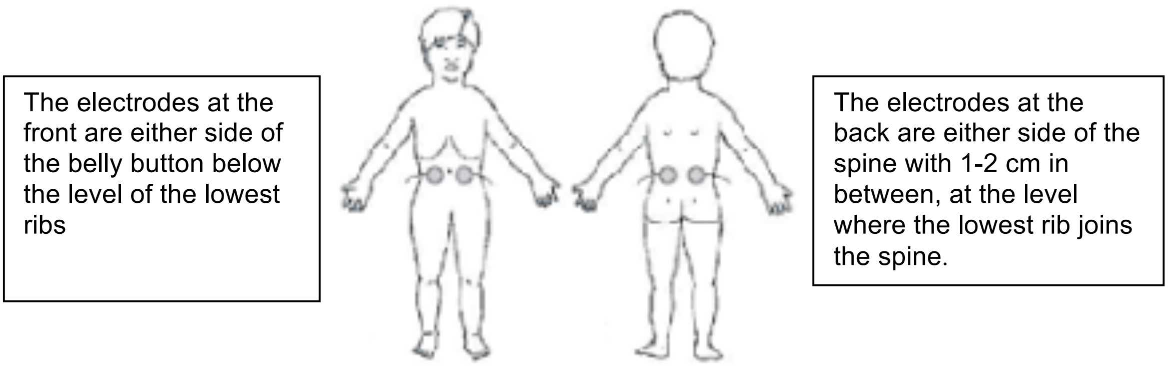
The initial assessment (week 0) took place at the Royal Children's Hospital and included a medical assessment of each child by a paediatrician and a continence physiotherapist (JC) of bowel dysfunction (including history, past medical management, neonatal/developmental issues, present bowel and bladder symptoms and management), routine measurements of weight, height, blood pressure and pulse rate (lying and standing) and assessment of faecal loading by abdominal palpation. A 4-week daily baseline bowel diary was commenced after explanation to the child and family of how to complete this. Written instructions were also given (see Appendices G & H)

Second Visit

On the second visit (end of week 4), Quality of life (QoL) was assessed using Pediatric Quality of Life Inventory (PedsQL). (see Appendices C & D)

Children were then randomised to receive either TENS or IFC stimulation on an alternating basis, that is, the first child enrolled in the study received a TENS machine and the second a IFC machine. This was documented and adhered to by the physiotherapist.

Parents were trained in the use of TENS or IFC by demonstration, and practised under supervision. This took approximately 15-30 minutes. They were given written instructions which explained the parts of the machine, the care of the electrodes, machine settings and instructions for use (see Appendices I & J). Stimulation was delivered by 2 channel TENS or IFC. The current was applied via four 50 x 50 mm self-adhesive conducting electrodes (Verity Medical Ltd. Hampshire S020 6BU, England). Two electrodes were placed either side of the spine in the curve of the back (T10-L2), each of these paired diagonally with two on the abdomen at the level of, and either side of the umbilicus. The position of electrodes was shown in a diagram in the written instructions for parents (see below).



The portable IFC was set at a beat frequency of 80 to 150 Hz. and current intensity set at a level that was above sensory threshold but quite comfortable and felt under all four electrodes. TENS current was biphasic rectangular pulses with a pulse width of 100μsec and frequency of 100Hz chosen to be as close as possible to the parameters used in the previous randomised controlled trial (see Chapter 3). Current intensity was the same as the portable IFC.

Both machines were used daily for 30 consecutive minutes. Families were told that while the machine was being used it was possible to move around quietly, watch TV or read, but not to actively play or go outside. Parents were instructed not to change laxative use during the trial.

Follow-up (week 20)

The daily bowel diary, including noting if treatment has been carried out, was continued during weeks 5-12 and during weeks 13-20. Phone contact was offered to the family throughout the trial to deal with problems that arose. A final hospital visit took place at the end of week 20. Questions were identical to those asked at the initial assessment and the PedsQL was re-administered.

4.3 Statistical analysis

This was a pilot study so we were interested in changes in individual patients. We compared the mean number of bowel actions, soiling episodes, and episodes of abdominal pain per week in the pre-treatment phase, the eight week treatment phase and the eight week post-treatment phase in each treatment group.

4.4 Results

Fifteen children were assessed for inclusion and eleven children aged 4-16 years (mean=9.2 years, SD 5.7) comprising six females and five males were recruited for this trial (see flow chart below). Of the four children who were excluded, one had intolerance to milk protein and improved once this was identified, and three children needed basic conservative treatment put in place again –they responded to these measures and no longer needed to be included in the study. One other child started in the study but withdrew due to reasons other than the intervention.

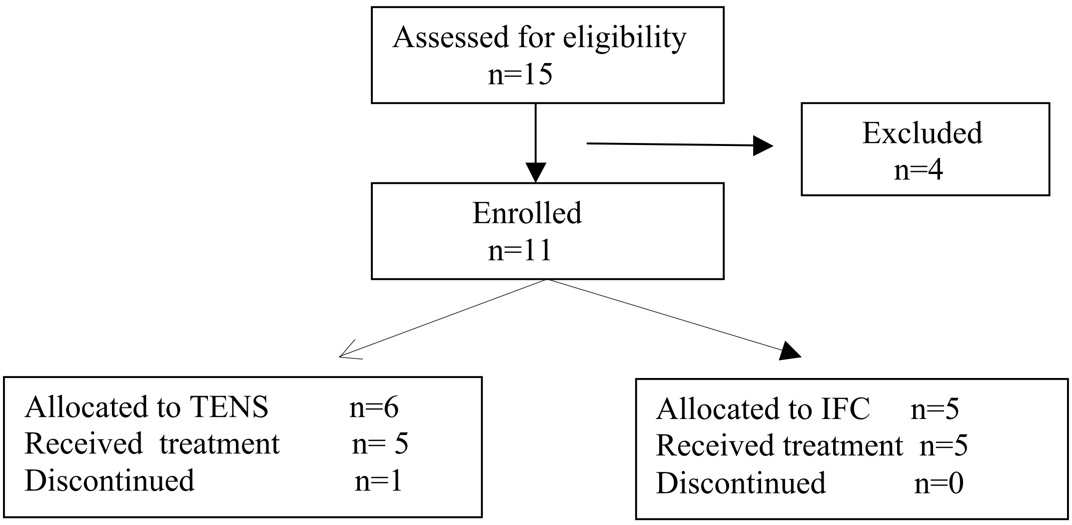


Figure 4.1 Flow chart of participants through the trial

All children had onset of symptoms between birth and aged four years. No child had an appendicostomy, however all had used stool softeners, osmotic agents, Movicol, and stimulants to treat symptoms. Three children had been admitted to hospital for bowel washouts via a naso-gastric tube and six had previously used enemas. One child in the TENS group had Attention Deficit Hyperactivity Disorder and one in the IFC group had moderate autism spectrum disorder. All children in the IFC group had soiling as did three in the TENS group. In regard to spontaneous or sense –related bowel actions, the TENS group appeared to have a higher average number per week (3.48±2.12) compared to the IFC group (1.00±1.59). The TENS group had less episodes of abdominal pain per week also. Eight of the ten children lived in outer regional and rural areas.

All families managed the use of the allotted machine without difficulty and no adverse events were reported. The only problem encountered on two occasions was insufficient care of electrodes or not changing electrodes when needed. This was easily managed by posting new electrodes to the family with minimal disruption to treatment.

Although the children and their families were assessed as being suitable for the study initially, it eventuated that four of the children recruited for this study had added difficulties which influenced and affected compliance. Three of the ten families underwent marital breakdown during the study. One child with autism spent a lot of time in respite care for reasons that were not apparent at the beginning of the trial. As stated one child withdrew from the study. Over the summer, compliance and data collection was affected by families being absent on holidays. Seven children and their families were compliant with treatment.

4.4.1 Sense-based (spontaneous) bowel actions

The average number of bowel actions per week precipitated by sensation over the 4-week pre-treatment phase, the 8-weeks treatment phase, and the 8-week post-treatment phase, is shown in Tables 4.2 and 4.3. Note that because all children did not adhere to the designated time periods, the actual number of treatment weeks for each child has been included in the Tables. Although there appears to be a trend to an increase in the average number of spontaneous bowel actions per week during the post-treatment phase in the IFC group, these data represents three of the five children only and are not conclusive.

While the average Bristol stool score is also indicated for each child, no group aggregate scores are included as the participants only intermittently recorded stool scores in their diaries, and these could not be completed retrospectively.

Table 4.2 Sense-precipitated bowel actions in IFC group participants. The mean Bristol stool score is given in brackets.

Case No.	Pre-Treatment		Treatment		Post-Treatment	
	No. of weeks	Mean No./Wk	No. of weeks	Mean No./week	No. of weeks	Mean No./week
1	4	1.00 (5.5)	9.86	1.73 (6.0)	8	2.50 (6.7)
2	4	0.00 (–)	4.00	0.00 (–)	–*	–
3	4	0.00 (–)	8.00	0.00 (–)	8	1.50 (5.33)
4	4	3.75 (3.0)	7.57	3.96 (3.5)	8	3.00 (–)
5	4	0.25 (–)	7.57	1.06 (4.0)	–*	–
Group	4	1.00±1.59	7.40	1.35±1.63	8	2.33±0.76

* Participant stopped participation

Table 4.2. Sense-precipitated bowel actions in IFC group participants. The mean Bristol stool score is given in brackets.

Table 4.3. Sense-precipitated bowel actions in TENS group participants. The mean Bristol stool score is given in brackets.

Case No.	Pre-Treatment		Treatment		Post-Treatment	
	No. of weeks	Mean No./Wk	No. of weeks	Mean No./week	No. of weeks	Mean No./week
1	3.29	4.67 (3.67)	9.29	4.95 (4.50)	8	4.13 (4.06)
2	4	0.00 (–)	10.57	1.14 (5.00)	8	0.88 (5.00)
3	4	4.00 (7.00)	11.00	2.82 (6.87)	8	3.63 (6.97)
4	4	6.25 (4.00)	9.00	6.11 (4.02)	8	6.88 (3.98)
5	4	2.50 (2.86)	8.00	0.38 (3.85)	–*	–
Group	3.86	3.48±2.12	9.57	3.08±2.44	8	3.88±2.46

* Participants stopped participation

The mean results from both groups are shown in Figure 4.2.

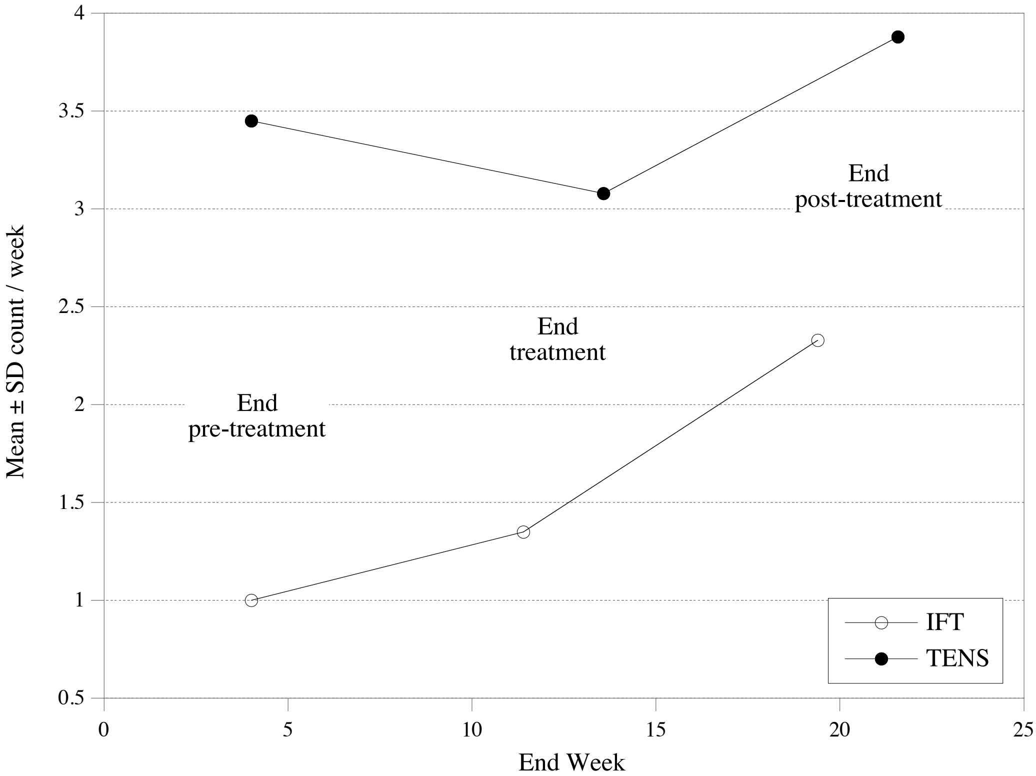


Figure 4.2 Change in incidence of sense-precipitated bowel actions following treatment in both participant groups.

4.4.2 Bowel actions without precipitating sensation

The average number of bowel actions per week without precipitating sensation over the pre-treatment, treatment and post-treatment periods is shown in Tables 4.4 and 4.5.

In the IFC group the average number of bowel actions without precipitating sense per week in the pre-treatment phase is skewed by the very high number of such bowel actions pre-treatment by participant number 1 in this group. There appeared to be no change in the average number of bowel actions without precipitating sense per week in either group.

While the average Bristol stool score is also indicated for each child, no group aggregate scores are included as the participants only intermittently recorded stool scores in their diaries.

Table 4.4 Bowel actions without precipitating sense in IFC group participants. The mean Bristol stool score is given in brackets.

Case No.	Pre-Treatment		Treatment		Post-Treatment	
	No. of weeks	Mean No./Wk	No. of weeks	Mean No./week	No. of weeks	Mean No./week
1	4	25.25 (–)	9.86	1.93 (6.84)	8	0.00 (–)
2	4	0.00 (–)	4.00	0.00 (–)	–*	–
3	4	0.50 (3.00)	8.00	0.38 (4.67)	8	0.50 (4.50)
4	4	0.00 (–)	7.57	0.00 (–)	8	0.00 (–)
5	4	0.00 (–)	7.57	0.00 (–)	–*	–
Group	4	5.15±11.24	7.40	0.46±0.84	8	0.17±0.29

* Participant stopped participation

Table 4.5 Bowel actions without precipitating sense in TENS group participants. The mean Bristol stool score is given in brackets.

Case No.	Pre-Treatment		Treatment		Post-Treatment	
	No. of weeks	Mean No./Wk	No. of weeks	Mean No./week	No. of weeks	Mean No./week
1	3.29	1.22 (4.25)	9.29	2.05 (4.04)	8	1.88 (2.47)
2	4	4.25 (5.00)	10.57	7.28 (4.73)	8	6.88 (4.53)
3	4	9.50 (7.00)	11.00	6.55 (6.81)	8	5.50 (7.00)
4	4	0.75 (–)	9.00	0.00 (–)	8	0.00 (–)
5	4	0.50 (3.00)	8.00	2.25 (4.06)	–*	—
Group	3.86	3.24±3.81	9.57	3.63±3.14	8	3.57±3.18

* Participant stopped participation

The mean results from both groups are shown in Figure 4.3

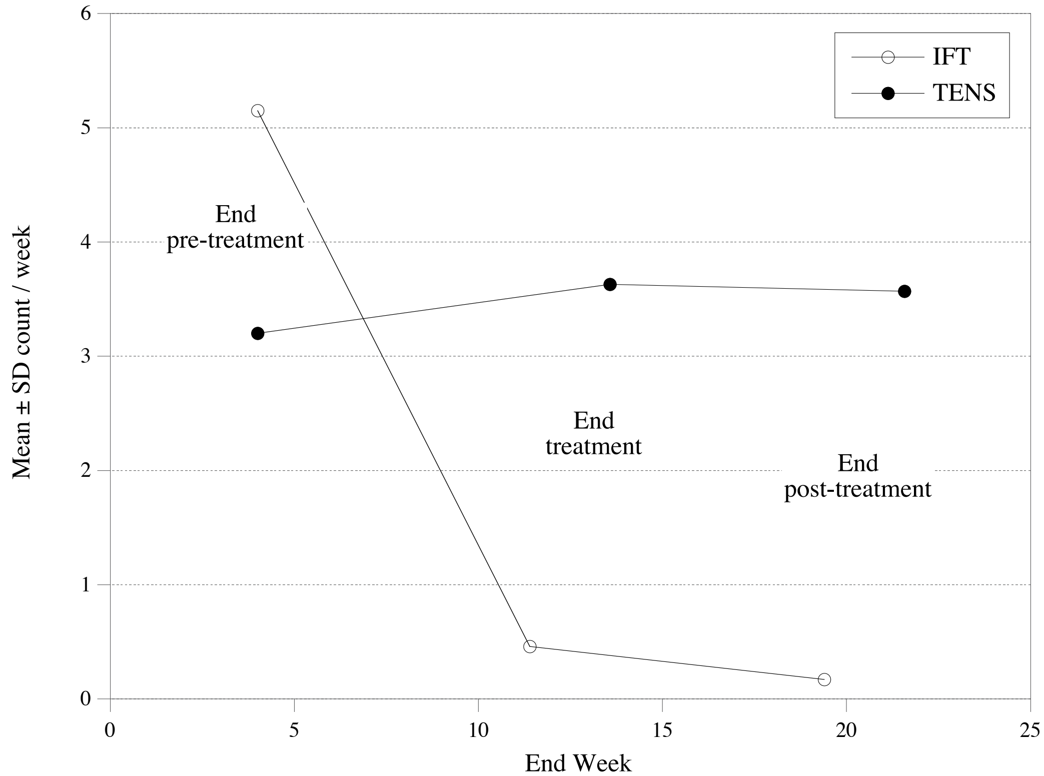


Figure 4.3 Change in incidence of bowel actions without precipitating sense following treatment in both participant groups.

4.4.3 Total bowel actions

The average number of total bowel actions per week, that is with and without precipitating sensation over the pre-treatment, treatment and post-treatment phases is shown in Tables 4.6 and 4.7.

In the IFC group the result was skewed by the very high number of bowel actions by participant number 1 in this group. If the pre-treatment results are considered without this participant, there was a trend to improvement in this group.

In the TENS group there was a small trend to improvement in the average number of total bowel actions per week.

Table 4.6 Bowel actions with and without precipitating sense in IFC participants. The mean Bristol stool score is given in brackets.

Case No.	Pre-Treatment		Treatment		Post-Treatment	
	No. of weeks	Mean No./Wk	No. of weeks	Mean No./week	No. of weeks	Mean No./week
1	4	26.25 (5.50)	9.86	2.74 (6.68)	8	2.50 (5.90)
2	4	0.00 (–)	4.00	0.00 (–)	–*	
3	4	0.5 (3.0)	8.00	0.38 (4.67)	8	2.00 (5.13)
4	4	3.75 (3.00)	7.57	3.96 (3.53)	8	3.00 (–)
5	4	0.25 (–)	7.57	1.06 (4.00)	–*	
Group	4	6.5±11.34	7.40	1.63±1.67	8	2.50±0.50

* Participant stopped participation

Table 4.7 Bowel actions with and without precipitating sense in TENS participants. The mean Bristol stool score is given in brackets.

Case No.	Pre-Treatment		Treatment		Post-Treatment	
	No. of weeks	Mean No./Wk	No. of weeks	Mean No./week	No. of weeks	Mean No./week
1	3.29	4.50 (3.77)	9.29	7.00 (4.27)	8	6.00 (3.57)
2	4	4.25 (4.91)	10.57	8.42 (4.76)	8	7.75 (4.65)
3	4	13.5 (7.00)	11.00	9.36 (6.83)	8	9.13 (6.99)
4	4	7.00 (4.00)	9.00	6.11 (4.02)	8	6.88 (3.98)
5	4	3.00 (3.73)	8.00	2.63 (4.05)	–*	
Group	4	6.45±4.20	9.57	6.70±2.60	8	7.44±1.33

* Participant stopped participation

The mean results from both groups are shown in Figure 4.4

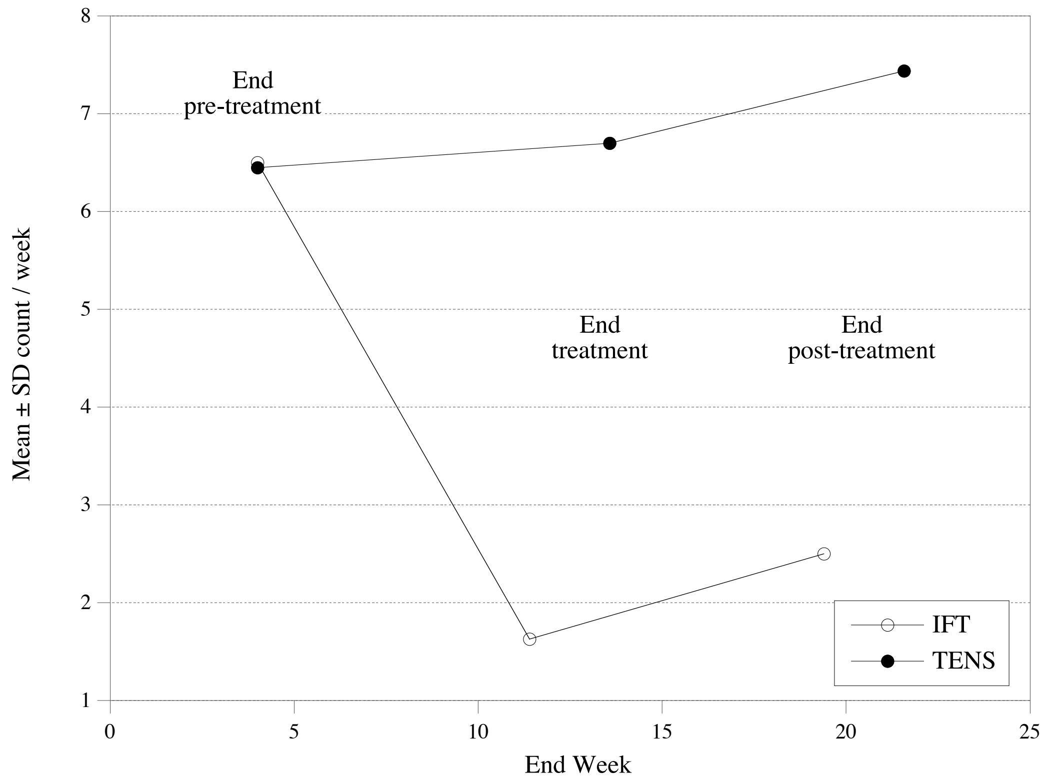


Figure 4.4 Change in incidence of bowel actions with and without precipitating sense following treatment in both participant groups.

4.4.4 'Stains' and 'scrapes'

The average number of stains and scrapes per week over the trial is shown in Tables 4.8 and 4.9. There was a small trend to improvement in the TENS group only.

Table 4.8 Stains (scrapes) in IFC group participants.

Case No.	Pre-Treatment		Treatment		Post-Treatment	
	No. of weeks	Mean No./Wk	No. of weeks	Mean No./week	No. of weeks	Mean No./week
1	4	4.50(10.00)	9.86	0.61 (5.27)	8	1.38 (8.63)
2	4	1.25 (5.00)	4.00	1.00 (6.00)	–*	–
3	4	1.75 (4.75)	8.00	3.13 (9.00)	8	4.38 (10.50)
4	4	0.75 (0.00)	7.57	0.13 (0.00)	8	0.00 (0.00)
5	4	0.00 (13.50)	7.57	0.00 (6.08)	–*	–
Group	4	1.65 ± 1.72 (6.65 ± 5.21)	7.40	0.97 ± 1.27 (5.27 ± 3.27)	8	1.92 ± 2.24 (6.38 ± 5.60)

* Participant stopped participation

Table 4.9 Stains (scrapes) in TENS group participants.

Case No.	Pre-Treatment		Treatment		Post-Treatment	
	No. of weeks	Mean No./Wk	No. of weeks	Mean No./week	No. of weeks	Mean No./week
1	3.29	0.00 (0.00)	9.29	0.11 (0.00)	8	0.00 (0.00)
2	4	4.00 (6.75)	10.57	6.91 (0.47)	8	4.38 (1.13)
3	4	0.00 (0.00)	11.00	0.00 (0.00)	8	0.00 (0.00)
4	4	0.50 (0.00)	9.00	0.00 (0.00)	8	0.00 (0.00)
5	4	0.00 (2.75)	8.00	0.00 (0.00)	–*	
Group	3.86	0.90 ± 1.75 (1.90 ± 2.96)	9.57	1.40 ± 3.08 (0.09 ± 0.21)	8	1.10 ± 2.19 (0.28 ± 0.57)

* Participant stopped participation

4.4.5 Abdominal pain

Tables 4.10 and 4.11 summarise the average number of days during which the participants experienced abdominal pain. There was a small trend to improvement in both groups.

Table 4.10 Mean number of days during which each participant in the IFC group experienced abdominal pain.

Case No.	Pre-Treatment		Treatment		Post-Treatment	
	No. of weeks	Mean No./Wk	No. of weeks	Mean No./week	No. of weeks	Mean No./week
1	4	1.50	9.86	0.71	8	1.63
2	4	6.75	4.00	3.00	–*	
3	4	2.00	8.00	2.38	8	0.75
4	4	3.75	7.57	3.83	8	1.75
5	4	0.00	7.57	0.00	–*	
Group	4	2.80 ± 2.58	7.40	1.98 ± 1.59	8	1.38 ± 0.55

* Participant stopped participation

Table 4.11 Mean number of days during which each participant in the TENS group experienced abdominal pain.

Case No.	Pre-Treatment		Treatment		Post-Treatment	
	No. of weeks	Mean No./Wk	No. of weeks	Mean No./week	No. of weeks	Mean No./week
1	3.29	1.22	9.29	0.54	8	0.00
2	4	0.00	10.57	0.00	8	0.00
3	4	1.75	11.00	2.09	8	1.75
4	4	3.5	9.00	1.78	8	0.75
5	4	0.25	8.00	0.00	–*	
Group	3.86	1.14 ±2.01	9.57	0.88±0.98	8	0.62±0.69

* Participant stopped participation

4.4.6 Quality of life

Table 4.12 shows those children for which complete pre- and post-treatment data exists. An unrecognised administrative error occurred resulting in incomplete data collection. No conclusions can be drawn from this data.

	Parent perceived QoL	Parent perceived QoL	Child perceived QoL	Child perceived QoL
Child/group	Physical domain, pre/post treatment	Psychosocial domain pre/post treatment	Physical domain, pre/post treatment	Psychosocial domain pre/post treatment
1. IFC	*	*	*	*
2. IFC	*	*	*	*
3. IFC	100 / 100	*	*	*
4. IFC	*	*	*	*
5. IFC	*	*	*	*
6. TENS	62.5 / 71.8	93.3 / 96.6	78.1 / 84.3	90 / 96.0
7. TENS	*	*	84.3 / 81.2	*
8. TENS	*	*	*	*
9. TENS	*	78.3 / 72.0	96.8 / 90.6	88.3 / 88.3
10. TENS	100 / 90	65.3 / 61.1	*	*

Table 4.12 PedsQL scores of parent and child perceived QoL. * missing data

4.5 Discussion

In this trial no-one had difficulty administering the treatment, no child complained of discomfort and there were no adverse events reported. Similarly to the group of parents who had previous repeated visits and observations of a physiotherapist administering transcutaneous electrical stimulation to their child, the parents in this study used TENS or IFC with no problems following 15-30 minutes of instruction only, endorsing the feasibility of these home-based interventions. It is unclear whether either treatment had an effect on bowel function.

Unfortunately the small number of participants and limited compliance with the diary made it impossible to draw strong conclusions from this pilot study. The same bowel diary had been used in the previous trial, with same instructions and compliance had not been an issue. Families of children with STC are used to keeping such diaries and it was considered that the lack of compliance in this pilot study was potentially due to two things. One is the multiple family issues that arose in the recruited cohort. The second was that not attending a physiotherapist three times weekly meant there was no reminder to complete the diary. In this pilot study several families verbally reported that they kept using the machine but didn't keep the diary, but we had no compliance indicator on the machines and relied on the recording of the level of intensity of current on the diary.

Compliance is affected by many factors. Suitability for participation in this study was assessed by a paediatrician and physiotherapist, and included the ability "of parents or child to report and document bowel habits"- that is the families were judged as having the ability to do so. It is well recognised that children with constipation and continence problems have co-morbid behavioural problems with consequent effects on the family and quality of life. It was not considered to exclude children/families on this basis, however whether a more structured social and behavioural assessment would alert researchers to potential difficulties needs consideration. Work on the brain-gut axis in adults is well-researched and is receiving attention in children more recently. It has been shown that children with constipation and faecal incontinence have increased responses in the central processing of emotions compared to healthy controls (von Gontard, et al., 2010). Understanding these emotional/behavioural difficulties and the social issues several families faced, it is not surprising that compliance was affected. In a future trial prompted weekly return of bowel diary pages by email or fax, for example, may enhance data collection in families living distant to treatment centres.

The groups were different in their baseline symptoms. This was particularly so in regard to spontaneous or sense –related bowel actions where the TENS group had a higher average number per week, and also less episodes of abdominal pain per week. The groups were too small to stratify according to symptoms. Participant number 2 in the IFC group skewed the number of bowel actions without precipitating sense as demonstrated in Figure 4.3. Children with STC are not a homogenous group but as yet we are unable to describe the sub-groups with authority. One sub-group appears to have more severe pain than most children with STC. Subject 2 had a high level of pain unless she had sufficient osmotic laxative to cause many loose bowel actions per day. This skewed results and in repeating this work thought needs to be given to more refined inclusion and exclusion criteria.

There is an insufficient number of participants who completed the protocol and although there were some small trends in both treatment groups (an increase in sense-precipitated bowel actions in the IFC group and total bowel actions in both groups, a decrease in ‘scrapes’ in the TENS group and abdominal pain in both groups), there is insufficient data to make any conclusions regarding effects on bowel function.

This study again highlights the difficulty of measuring the effect of transcutaneous electrical stimulation on bowel function. Each outcome variable can reflect different parameters. For example, the number of bowel actions alone can be misleading as it does not indicate the amount of bowel content evacuated or what is left behind. The number of bowel actions may not change but soiling may reduce which may indicate that each bowel action is more complete. The number of bowel actions may increase but soiling may not change as rectal emptying and perception take longer to recover. Each variable needs to be measured in relation to the others therefore. The development of a composite score of defaecation frequency, soiling, rectal perception, abdominal pain and laxative use would greatly enhance this area of research.

To establish the effect of home-based portable IFC and TENS requires this work to be repeated with improved randomisation and due attention the issue of compliance for distant families. The development of a composite outcome measure may improve the measurement of effect of the interventions.

4.6 References

Ismail, K. A., Chase, J., Gibb, S., Clarke, M., Catto-Smith, A. G., Robertson, V. J., Hutson, J., Southwell, B. (2009). Daily transabdominal electrical stimulation at home increased defaecation in children with slow-transit constipation: a pilot study. *Journal of Pediatric Surgery, 44*(12), 2388-2392.

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Von Gontard, A., Schneider, A., El Khatib, D., Schreiner-Zink, S., & Rubly, M. (2010). *Central Nervous System processing of emotions in children with fecal incontinence; further evidence for the brain-gut axis.* Paper presented at the 1st World Congress of Paediatric Urology, San Francisco.

CHAPTER 5: PREFACE

Previous research on Slow Transit Constipation have not considered whether there might be a musculo-skeletal component which can be assessed and treated. The process of defaecation is dependent on the inter-related function of bowel motility and the use of abdominal, other trunk and pelvic floor muscles. The pelvic floor muscles act in synergy with abdominal, chest wall, spinal muscles and the respiratory diaphragm, to generate and maintain intra-abdominal pressure and spinal stability. If there are differences in the trunk musculoskeletal control in children with STC, there could be potential for interventions to produce more-effective use of the voluntary defaecatory muscles, as well as the use of interferential current to improve bowel motility.

This study aimed to determine if children with STC have different trunk musculoskeletal characteristics that might be related to their defaecation difficulties, compared to controls.

This chapter presents a study which has already been published:

Chase, J. W., Stillman, B. C., Gibb, S. M., Clarke, M. C., Robertson, V. J., Catto-Smith, A. G., Hutson, J. M., Southwell, B.R. (2009). Trunk strength and mobility changes in children with slow transit constipation. *Journal of Gastroenterology and Hepatology, 24*(12), 1876-1884.

The format has been changed to be consistent with this thesis but the content is unaltered.

CHAPTER 5: TRUNK STRENGTH AND MOBILITY CHANGES IN CHILDREN WITH SLOW TRANSIT CONSTIPATION.

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Funding source: National Health and Medical Research Council, Australia (Trial registration No 384434)

Ethics granted Royal Children's Hospital Ethics Committee (EHRC 23040 C) (Appendix K)

5.2 Abstract

Background and Aim

It appears that there are no published reports on childhood Slow Transit Constipation (STC) that have considered the state of the musculoskeletal components of the trunk in these children. This study aimed to determine if children with STC have different trunk musculoskeletal characteristics that might be related to their defaecation difficulties, compared to controls.

Methods

With the aid of computer-analysed photographs and clinical testing, 41 children with STC and 41 age-matched controls were examined for Marfanoid features, sitting posture, spinal joint mobility and trunk muscle strength. The latter was assessed by measuring maximum voluntary abdominal bulging and retraction in sitting, and active trunk extension in prone-lying. Levels of general exercise and sedentary activities were evaluated by questionnaire.

Results

STC subjects were more slumped in relaxed sitting ($p \leq 0.001$), less able to bulge ($p \leq 0.03$) and less-able to actively extend the trunk ($p = 0.02$) compared to controls. All subjects sat more erect during abdominal bulging ($p \leq 0.03$).

Conclusion

The results show that STC children have reduced trunk control and posture, which indicates that clinicians should focus on training of trunk muscles and correction of sitting posture. There was no evidence that children with STC exercised less than the controls.

5.3 Introduction

Slow transit constipation (STC) is an idiopathic disorder characterised by slow transit of contents along the entire length of the colon (Benninga, et al., 1996; Hutson, et al., 2004). Hypotheses as to causes range from primary (developmental) dysfunction to hormonal disorders. Five to 10% of families have more than one member affected (Hutson, McNamara, Gibb, & Shin, 2001). Dysfunctional enteric nervous system, decreased levels of substance P, decreased numbers of Interstitial cells of Cajal and connective tissue disorders have all been implicated (Reilly, et al., 2008; Shin, Southwell, Stanton, & Hutson, 2002; Treepongkaruna, et al., 2001).

Despite aggressive treatment, including the formation of an appendix stoma through which antegrade bowel washouts are performed, faecal incontinence, recurrent faecal impaction, reduced or absent rectal sensation and abdominal pain remain as significant physical, social and emotional consequences for the child and family. A low quality of life has also been demonstrated (Clarke, et al., 2008).

There is little information on possible musculoskeletal associations with STC. We compared 39 STC children aged 7 – 17 years with 41 age- and gender-matched controls, and found a higher rate of generalised joint hypermobility (GJH) in boys within the STC group as compared to boys with GJH in the control group (Reilly, et al., 2008). De Kort and colleagues (2003) investigated non-neurogenic bladder sphincter dysfunction and constipation in 89 GJH children aged 5 – 12 years, and 116 age-matched controls. They found no significant difference in the prevalence of constipation or faecal incontinence in the females, however constipation was significantly more prevalent in the hypermobile males (p = 0.02). Faecal incontinence was also more common in the hypermobile males, but not significantly so (p = 0.07).

Adib and colleagues (2005) also reported a relationship between GJH and childhood chronic constipation and faecal incontinence; but without statistical support. Subsequently Adib (2006) indicated that approximately 30% of children with GJH in his paediatric rheumatology clinic have a history of chronic constipation (contrast 11.2% of control participants in de Kort's 2003 study).

The process of defaecation is dependent on the inter-related function of abdominal, other trunk and pelvic floor muscles (PFM) (Sapsford & Hodges, 2001). The PFM act in synergy with the abdominal and chest wall muscles, the deeply placed multifidus, and the respiratory diaphragm, and may be likened to a plastic pressurised abdominal cylinder that generates and maintains intra-abdominal pressure and spinal stability (Hodges, 1999). If there are differences in the trunk musculoskeletal control in children with STC, there could be potential for interventions to produce more-effective use of the voluntary defaecatory muscles.

5.4 Aims

The purpose of the study was to determine whether a sample of children and adolescents with STC had trunk musculoskeletal characteristics different from age- and sex-matched control participants. Additional aims were to determine the usual activity patterns of STC children.

5.5 General Methods

Ethics approval for this study was given by the Royal Children's Hospital, Melbourne (HREC 23040C) (see Appendix K). All participants were aged 7 – 18 years. Written informed consent was obtained from one parent of each participant, and verbal consent was obtained from every participant.

5.5.1 Participants

Based on a preliminary power analysis, it was determined that 40 participants with STC should be studied along with 40 control participants. Participants in both groups were matched for age and sex. Since the STC group had a majority of males, the control group was selected so as to have a comparable male bias.

The selection criteria for the STC participants were a diagnosis of STC by radionuclear transit studies (Cook, et al., 2005), and at least a two-year history of medical management. Hirschsprung's disease, coeliac disease and endocrine abnormalities were excluded by appropriate testing. Control participants were recruited by requests for volunteers from Australian Scouting groups predominantly, and children of colleagues. Parents of these volunteers confirmed at interview their children had no known relevant musculoskeletal disorders, and no history of constipation requiring medical management.

5.5.2 Photography and computer analysis

Photographs were first obtained using a tripod-mounted digital camera. All images were then transferred to a computer, *straightened* relative to any convenient vertical or horizontal line in the background of the photo (e.g. wall-floor horizontal, or wall-wall vertical), cropped, then subjected where necessary to normalisation of grey-scale levels, gamma correction, and enhancement of brightness, contrast and colour saturation; all using ImageJ software (http://rsb.info.nih.gov/ij/)

ImageJ was also used to measure the linear distances and joint angles required for various analyses. A ruler of known length was included in all photographs to allow calibration of the linear measures in centimetres.

All sitting measures were made with the participants sitting on the same stool with a fixed height (42 cm) approximating the usual height of a toilet seat. Since everyone typically uses the same height toilet seat, the stool height was not adjusted to accommodate the different heights of the participants.

5.5.3 Specific methods

5.5.3.1 Marfanoid tendency

Each participant was asked to encircle each wrist with the thumb and middle finger of the opposite hand. The results were expressed as thumb and finger did not meet, touched, or overlapped. Overlapping, which signifies relatively long fingers, is a positive Marfanoid sign, as is an upper limb span-to-height ratio > 1.03; where > 1.0 indicates relatively long upper limbs (Grahame & Hakim, 2008). A posterior view photograph was taken of each participant standing in bare feet with both upper limbs outstretched sideways to form a "T".

5.5.3.2 Passive trunk flexion-extension

For extension, each participant was positioned in prone-lying with their hands on the couch at shoulder height (Figure 5.1a). They were then asked to push up with the hands as far as comfortable while keeping the pelvis on the couch. This end-position, which represents combined passive thoracolumbar and hip extension, was computer-measured as the angle between a line representing the long axis of the thigh, and another line forming a tangent to the upper thoracic spine.

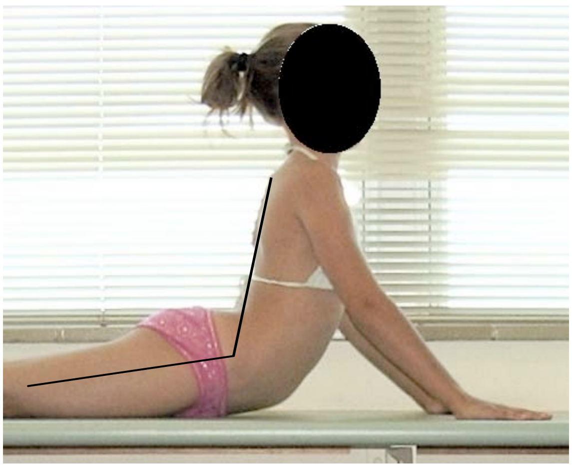


Figure 5.1a Passive trunk extension

For measurement of combined thoracolumbar and hip flexion, a lateral photograph was taken of each participant attempting to place their hands flat on the floor whilst standing upright with the knees straight (Figure 5.1b). The end-position was measured as for passive trunk extension.

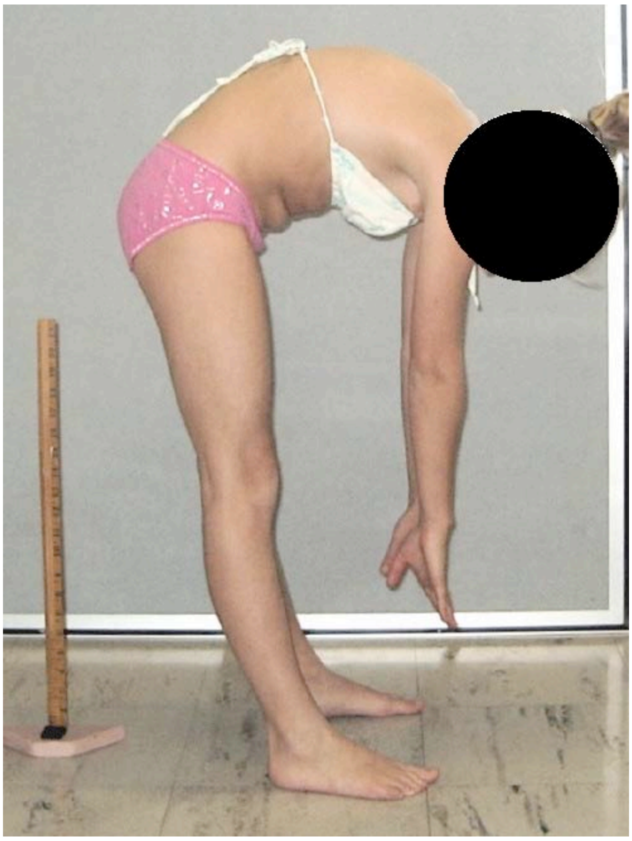


Figure 5.1b passive trunk flexion

5.5.4 Sitting posture

Sagittal-plane sitting posture was assessed from lateral photographs of each child by computer-based measurement of sacral tilt and thoracolumbar flexion-extension. Measurements were obtained whilst the child sat on a 42 cm high stool with one upper limb supported forward (by placing the hand on the back of a chair) (Figure 5.2 – see below). This served to expose the abdomen for the measurements taken: (1) while sitting relaxed, (2) at the end of maximum voluntary abdominal bulging, and (3) at the end of maximum voluntary abdominal retraction (Figure 5.2 – see below).

5.5.5 Trunk extension strength

For trunk extension assessment, each participant was positioned in prone lying with their upper limbs outstretched above the head, and lower limbs stabilised on the couch by an assistant (Figure 5.1c). Each participant was asked to lift (arch) the back as high as possible. The range of this active movement was measured as for passive trunk extension.

Figure 5.1c Active trunk extension

5.5.6 Abdominal muscle strength/control

Maximum voluntary abdominal bulging and retraction were measured through a transverse plane at the junction of the lower one-third and upper two-thirds of the trunk. The surface anatomy for this measurement was developed by one of the authors (BCS) based on a consideration of anatomical (skeletal) data and some empirical clinical trials. Figure 5.2a shows the method employed with reference to one seated participant in the relaxed abdominal state.

A spherical reflective reference marker was placed so as to identify the suprasternal notch, the plane of which is labelled 'SN' in Figure 5.2a. This was deemed to be the upper limit of the trunk. The greater trochanter in the seated subject was deemed to be equivalent to the pubic symphysis and, thus, the lower limit of the trunk. This plane is shown as 'GT' in the Figure. Since the junction of the upper one-third and lower two-thirds of the distance between 'SN' and 'GT' approximates the xiphisternum (the upper limit of the abdomen), the mid-point between 'SN' to 'GT' approximates the mid-abdominal plane ('MA' in the Figure), This was the level chosen for measuring the anteroposterior distance during bulging and retraction.

The scaling rod included in all the photographs (see Figure 5.2), allowed calibration of the magnitude of bulging and retraction at the mid-abdominal level in centimetres. This distance was also calculated as a percentage of the relaxed anteroposterior abdominal diameter to standardise for variations in trunk girth between the participants.

Figure 5.2 (a) (b) (c) Seated participant with right arm forward (hand resting on a chair)

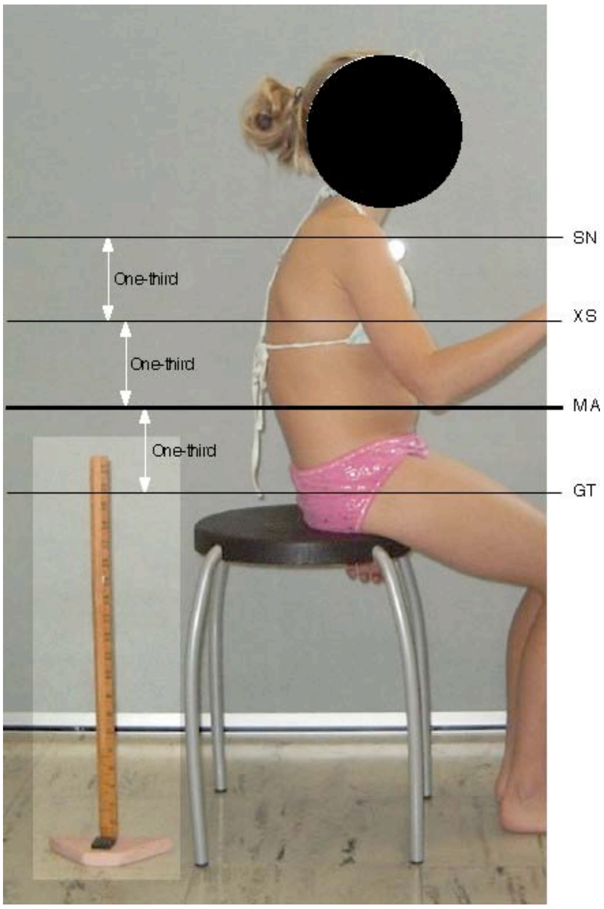


Figure 5.2 (a) Relaxed abdomen

(a), SN = plane of suprasternal notch, GT = plane of greater trochanter (= pubic symphysis), XS = plane of xiphisternum (junction of upper 1/3 and lower 2/3 of distance SN to GT), and MA = plane of abdomen (junction of lower 1/3 and upper 2/3 of distance SN to GT).

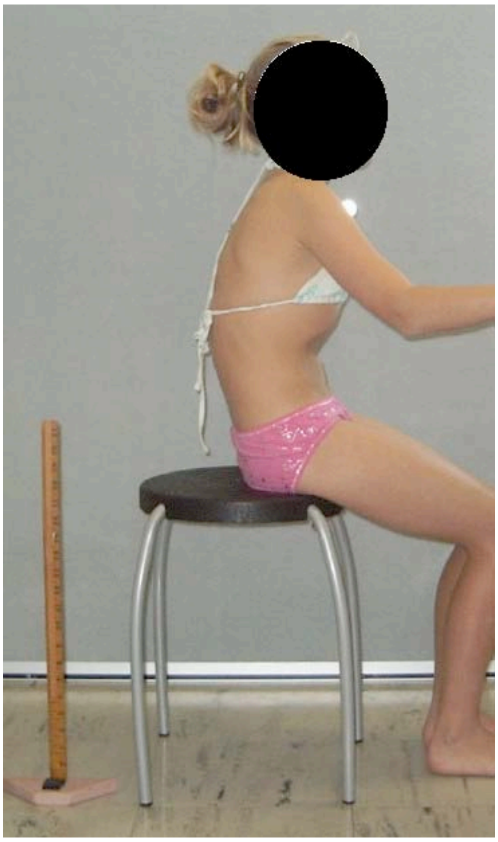


Figure 5.2(b) Maximum voluntary retraction

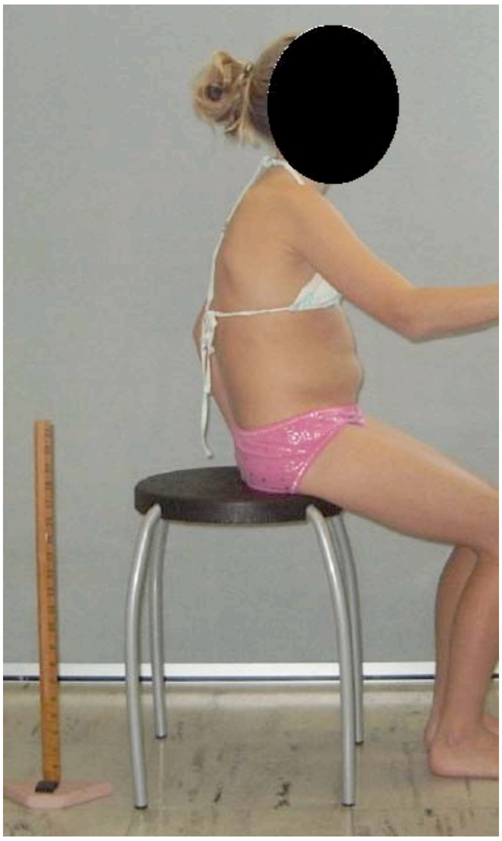


Figure 5.2(c) Maximum voluntary bulging

5.5.7 Activity levels

The average hours per week of physical activity (eg. walking, cycling, bike-riding and sport) and sedentary activity (ie., television viewing and computer activities) outside of school time at the time of assessment was determined by interview.

5.5.8 Statistical methods

The numerical results derived from computer-aided measurement of photographs and the interview-based measurement of activity levels, were initially analysed by descriptive statistics. Following analysis of scatterplots comparison between related data sets were then made by linear, and where appropriate, non-linear correlations, t-tests and repeated measures analysis of variance. Based on clinical observations it was expected that the STC group would have reduced active trunk mobility, flexed sitting posture and decreased abdominal control.

5.6 Results

5.6.1 Participant groups

Table 5.1 shows that the participants in the STC and control groups were matched for number of subjects, age, sex, BMI, body weight as a percentile of normal, and Marfanoid characteristics.

Table 5.1 Subject characteristics

Variable	STC group	Control group	Statistics
Number of subjects	41	41	
Age (mean ± SD)	11.7 ± 2.7	11.8 ± 2.4	t-test, $p = 0.90$
Females [males]	11 [30]	15 [26]	Chi-Sq, $p = 0.34$
BMI (mean ± SD)	20.2 ± 4.2	19.2 ± 2.8	
Body weight as percentile*	66.4 ± 31.8	59.8 ± 24.0	t-test, $p = 0.30$
Wrist encircling overlap (count (%))	17 (41.5)	17 (41.5)	
Upper limb / height ratio > 1.03 (count (%))	3 [7.9)	4 (9.8)	

- From standardised percentile curves accessed at http://kidshealth.org/parent/nutrition_fit/nutrition/bmi_charts.html

5.6.2 Trunk Mobility

Mobility of the trunk calculated for each participant as the sum of the obtained ranges of passive trunk flexion and extension, averaged 205.1 ± SD 16.5 degrees in the STC group, and 210.2 ± SD 16.2 degrees in the controls. There was no significant difference between the two participant groups with respect to trunk mobility thus measured (unpaired t-test, $p = 0.17$). An unpaired t-test also revealed no significant difference between in the range of passive trunk extension (STC group = 57.0 ± SD 9.8 degrees, controls = 58.6 ± SD 8.2 degrees, $p = 0.41$) or passive trunk flexion (STC = 148.1 ± SD 11.9 degrees, controls = 151.8 ± SD 11.3 degrees, $p = 0.15$).

The female participants had a greater range of passive trunk extension (STC = 63.1 ± SD 6.4 degrees, controls = 53.4 ± SD 9.0 degrees, $p = 0.0001$), and a greater total range of flexion-extension (STC = 215.2 ± SD 15.1, controls = 204.0 ± SD 15.8 degrees, $p = 0.01$), but not passive flexion (STC = 152.2 ± SD 12.9 degrees, controls 148.9 ± SD 10.9 degrees, $p = 0.37$).

5.6.3 Sitting posture

Table 5.2 summarises the anteroposterior pelvic tilt and thoracolumbar flexion-extension posture measured as the participants sat with one upper limb forward.

To determine whether the forward-supported upper limb influenced the natural sitting posture of the participants, all of the STC participants (41) and most of the control group (30 of 41) also had their sitting posture measured with both upper limbs relaxed by their side. The mean pelvic tilt for all participants changed from -10.3 ± 9.3 degrees when both arms were by their side, to -10.7 ± 9.7 degrees with one upper limb forward. This change was not significant ($p = 0.57$). The corresponding values for thoracolumbar flexion were 43.2 ± 18.1 and 39.6 ± 18.6 degrees; that is the thoracolumbar spine extended by on average 3.6 degrees when one arm was lifted forwards. Albeit small, this difference was statistically significant ($p = 0.03$), but it was not considered clinically significant because it may have been due to measurement error.

Table 5.2 Mean ± SD pelvic tilt and thoracolumbar flexion angles during sitting with relaxed, bulged and retracted abdomen.

Group	Sitting relaxed one arm forward		Sitting with bulging		Sitting with retraction	
	Plvc tilt*	ThLbr* Flex	Plvc tilt	ThLbr Flex	Plvc tilt	ThLbr Flex
STC	-13.1 ± 9.8	46.2 ± 17.4	-9.5 ± 10.1	35.8 ± 16.1	-12.5 ± 10.5	41.7 ± 18.7
Controls	-8.9 ± 9.9	33.12 ± 18.1	-5.0 ± 9.7	27.0 ± 16.8	-8.8 ± 8.8	32.2 ± 14.2

- Plvc = pelvic, ThLbr = thoracolumbar; -ve pelvic tilt = upward / posterior tilt, as in slumped sitting (see Figure 3), +ve tilt = downward / anterior tilt, as in erect sitting (see Figure 3); +ve thoracolumbar angle = flexed thoracolumbar spine.

Figure 5.3a and 5.3b illustrate the extremes of the two observed types of sitting posture we found. In (a) the pelvis is tilted negatively (upwards / backwards) by 24.3 degrees, and the thoracolumbar spine flexed 42.8 degrees to form a slumped (C-shaped) sitting posture. In (b) the pelvis is tilted positively (downwards / forwards) by 11.2 degrees, which creates an S-shaped lumbothoracic spine and erect sitting posture.

Figure 5.3 (a) (b) Two of the STC participants showing how the relaxed sitting posture (with one hand supported forward) is determined by a combination of pelvic tilt and thoracolumbar flexion.

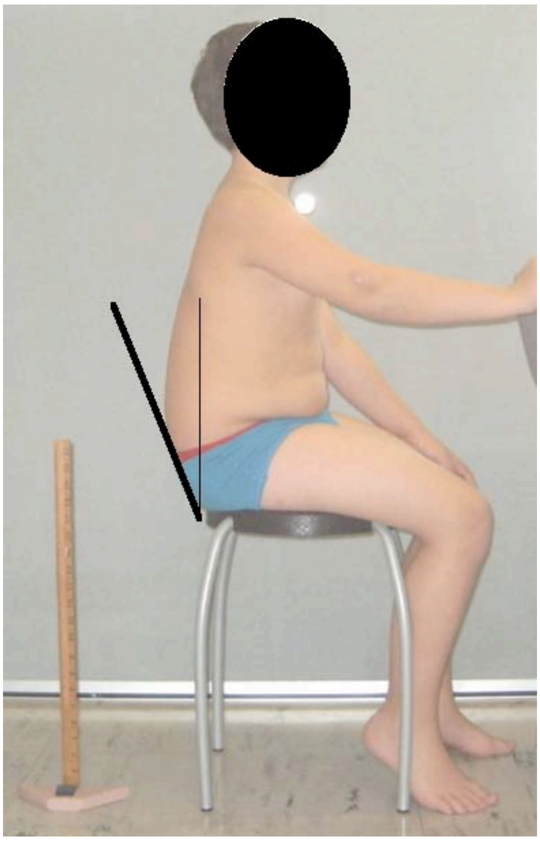


Figure 5.3 (a) Shows a negative pelvic tilt combined with a large thoracolumbar flexion to create a typical slumped posture.

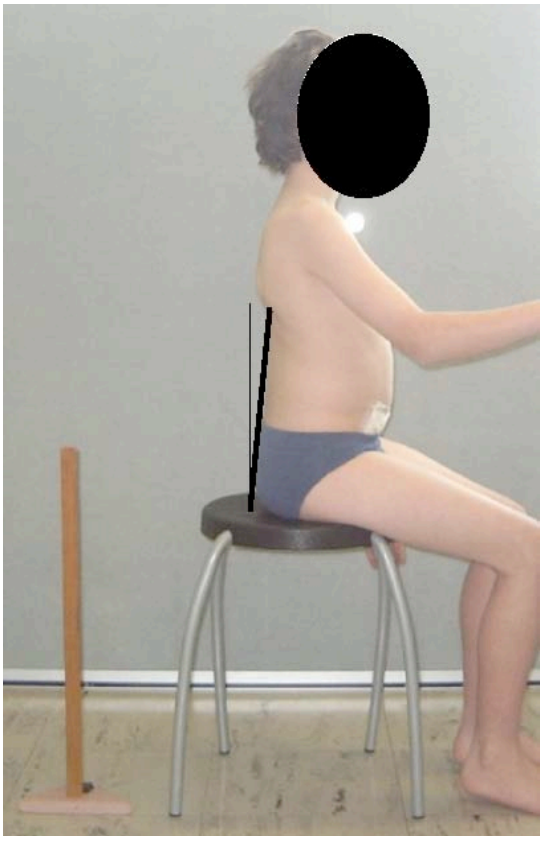


Figure 5.3 (b) Shows a positive pelvic tilt combined with a small thoracolumbar flexion to create an erect posture. The bold lines approximate the plane of the sacrum (and indirectly, pelvic inlet). The subtended fine lines represent the vertical plane. See text for further detail.

A two-way ANOVA considering sitting status (relaxed, bulging and retracting abdomen) revealed a significantly more positive pelvic tilt ($p = 0.001$), and less flexed thoracolumbar spine ($p = 0.0001$) in the control subjects; that is, the control group sat more upright under all test conditions.

5.6.4 Abdominal bulging and retraction

Figure 5.2b and 5.2c shows one child's ability to voluntarily and maximally retract the abdomen. Table 5.3 shows the mean ± SD anteroposterior abdominal diameter at rest, during bulging and during retraction, along with the differences between bulge and rest, and retract and rest.

Table 5.3 Mean ± SD anteroposterior diameter (in cm) of the abdomen at rest, during maximum voluntary bulging, and during maximum voluntary retraction in the two subject groups.

Measure	Sitting with one arm supported forward		
Measure	Relaxed sitting	Bulging	Retraction
STC	15.5 ± 2.5	16.0 ± 2.6	12.8 ± 2.3
Controls	13.9 ± 2.0	14.6 ± 2.1	11.3 ± 2.0

A t-test showed that the relaxed anteroposterior diameter was significantly greater in the STC subjects under all three test conditions (relaxation p = 0.001, bulge p = 0.01 and retract p = 0.002).

Since the capacity to bulge and retract may have been proportional to the resting abdominal anteroposterior diameter, an analysis was made of the capacity to bulge and retract, represented as a percentage of the resting anteroposterior diameter (Figure 5.4). Linear curves of best fit show that there is a negligible direct correlation between resting anteroposterior diameter, and the ability to bulge ($r^2 = 0.05$) and retract ($r^2 = 0.01$).

The STC participants bulged by an average 2.8 ± 4.6% relative to the resting diameter; whereas the control subjects bulged 5.1 ± 5.0%. This difference was significant (p = 0.03). The STC participants retracted 17.5 ± 5.4%, whilst the control participants retracted 18.8 ± 7.6%. This difference was non-significant (p = 0.40).

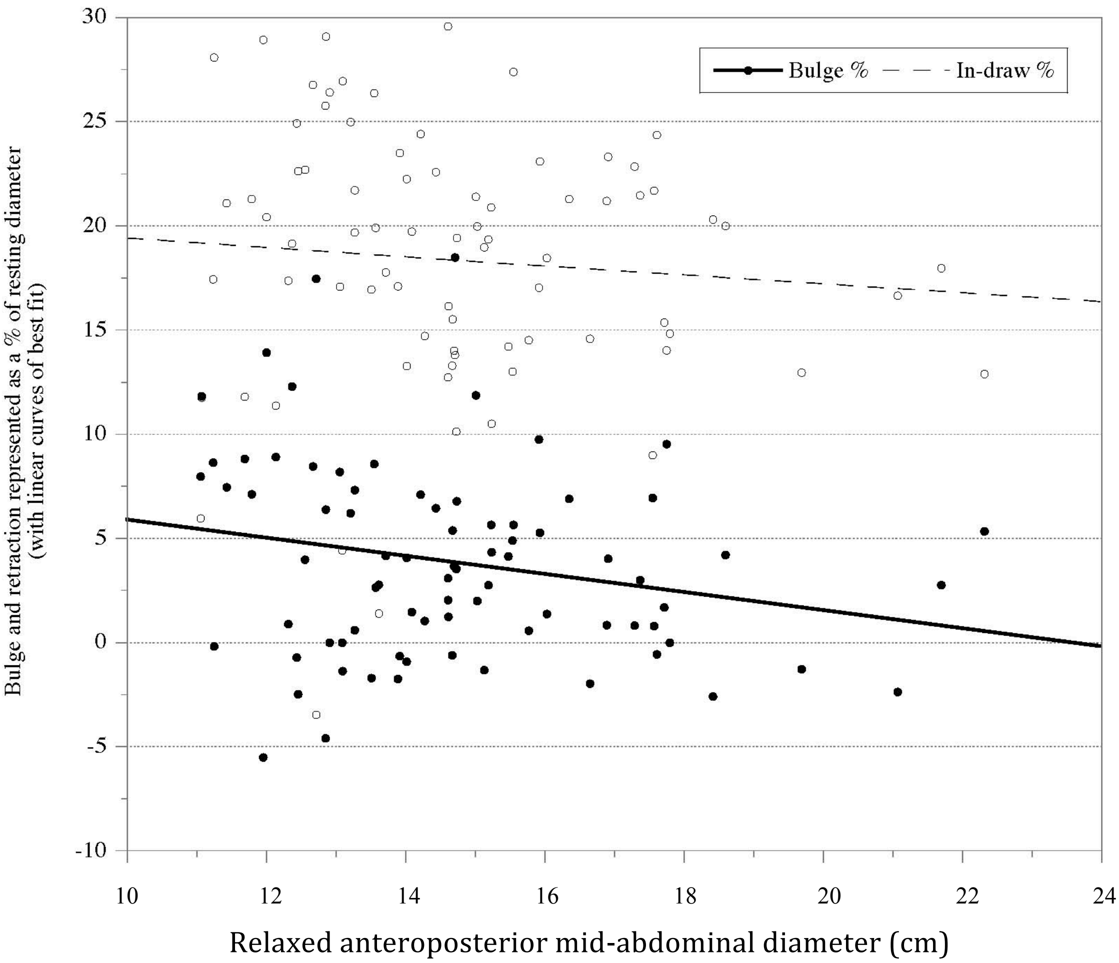


Figure 5.4 Scatterplot with linear regression curves showing an non-significant relationship between the resting anteroposterior abdominal diameter and the ability to bulge and retract; the latter measured as the bulge and retract diameters represented as a percentage of the resting diameter).

5.6.5 Active trunk extension

The maximum range of active trunk (hip and thoracolumbar) extension in the STC participants was 23.4 ± 10.3 degrees, whilst the corresponding value in the control subjects was 29.3 ± 11.2 degrees. A t-test confirmed the significantly greater capacity in the control participants ($p = 0.02$).

5.6.6 Usual activity levels

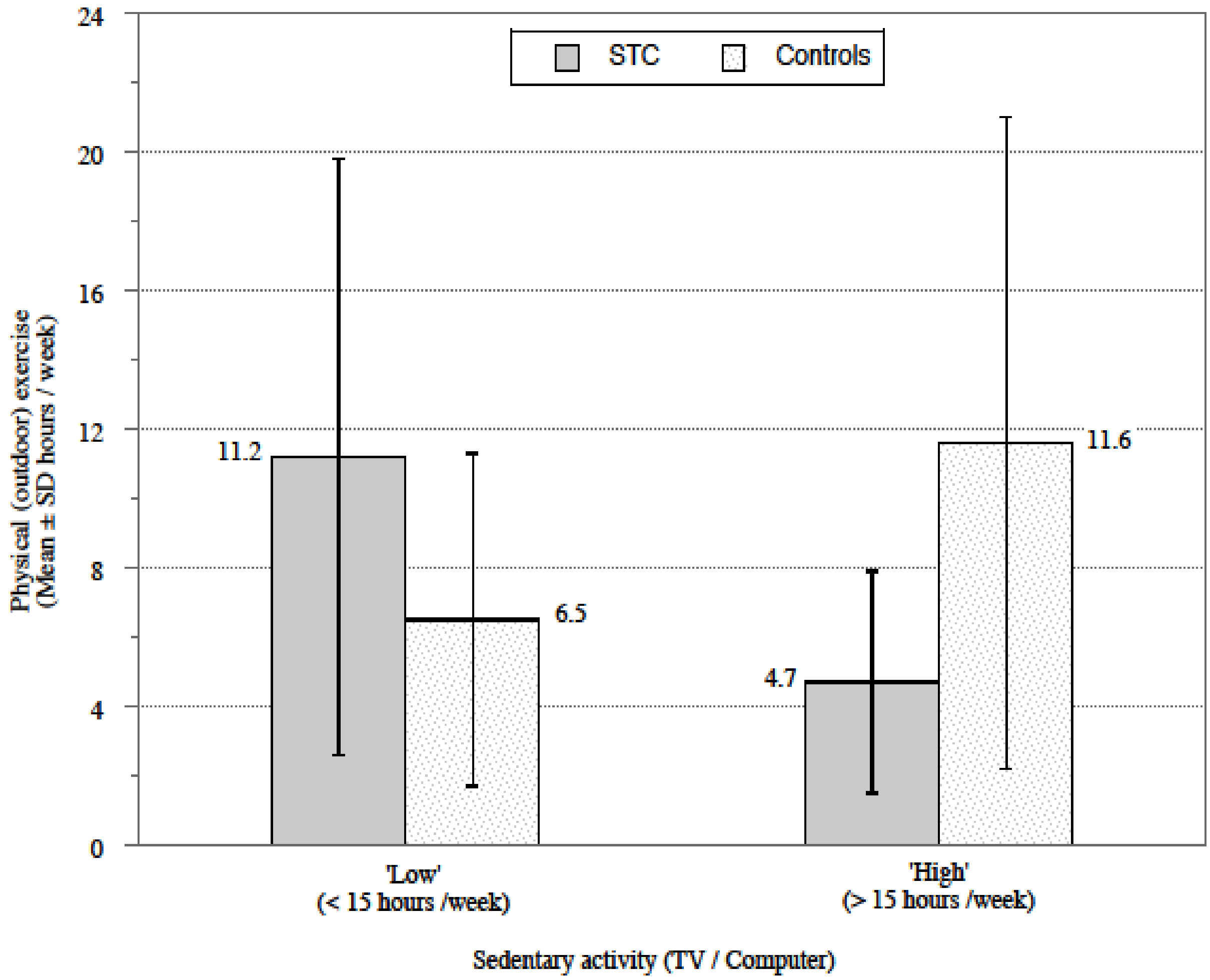
Table 5.4 shows the average hours of physical and sedentary (TV/computer) activities outside of school hours per week by the participants in each group.

Table 5.4 Activity levels in mean hours / week for the STC and control participant groups

Activity	STC group	Control group	Statistics
Exercise	9.8 ± 8.2	7.7 ± 6.9	t-test, $p = 0.21$
Sedentary	13.6 ± 8.4	12.3 ± 8.9	t-test, $p = 0.50$

Figure 5.5 shows the relationship between physical and sedentary activity in the two participant groups based on categorising the sedentary activity time as low (< 15 hours / week) or high (> 15 hours / week). The graph shows that the STC participants who participated in relatively high levels of physical activity, typically had low sedentary activity hours. The control participants with high sedentary hours also had high physical activity hours. The control participants with low sedentary activity hours also had relatively low physical activity hours. A two-way ANOVA confirmed an interaction effect between physical and sedentary hours in the STC and control groups ($p = 0.002$).

Figure 5.5 Relationship between physical and sedentary activity in both participant groups based on categorising sedentary activity as low (< 15 hours / week) or high (> 15 hours / week).



5.7 Discussion

We know of no other studies of the trunk musculoskeletal characteristics in children with STC apart from those papers noted in the introduction relating to generalised joint hypermobility (Adib, et al., 2005; de Kort, et al., 2003; Reilly, et al., 2008). In the present study the STC and control participants were not significantly different in age, sex, body mass index, or Marfanoid tendency; therefore the results in this study are unlikely to have been significantly determined or influenced by these factors.

It might be argued that the control participants, being largely from the Scouting Association, might be physically more active than the average "normal" child. The two reasons we do not agree with this are that the control participants were largely accessed from Scouting Jamborees which were attended by a wide range of children for diverse backgrounds. Secondly, current scouting activities involve as many sedentary as physical activities. This is supported by our finding of no significant difference in BMI.

5.7.1 Defaecation posture

Notwithstanding the widely held view that squatting is the optimum posture for defaecation (Sikirov, 2003); the fact remains that there are many instances, including the rarity of squatting toilets in Western Societies, where this is impractical and the sitting defaecation posture must be used.

The act of defaecation is a complex interplay between autonomic and somatic systems. In regard to the latter, an upright and forward leaning sitting position has been said to facilitate defaecation by lengthening the anal aperture and widening the ano-rectal angle (Tagart, 1966). Ideally, if sitting posture is correct and faecal consistency normal, expulsion occurs, in the main, by rectal propulsion once sphincter release has occurred. If added voluntary effort is needed, transversus abdominis assists by increasing intra-abdominal pressure, as does the internal and external oblique muscles, the diaphragm, and to a lesser extent rectus abdominis. If action of these abdominal muscles is maintained with an open glottis then spinal stability is also enhanced (Shirley, Hodges, Eriksson, & Gandevia, 2003).

In the present study, the control subjects had a more extended thoracolumbar spine than the STC subjects in all three sitting states examined (relaxed, bulging, and retraction). Based on the abovementioned view of Tagart (1966), the STC participants had a less-than-optimum posture during defaecation. This finding points to the logic of attempting to improve defaecation posture in STC children.

5.7.2 Trunk muscle strength /control

In addition to postural differences, there were significant differences in the results from the muscle strength /control assessments. Although electromyography was not used in this study, previous electromyography studies by Shirley (2003) and Sapsford (2001) attribute respiratory diaphragm muscle contraction with relaxation of the abdominal wall to the maximum voluntary bulging action; and voluntary contraction of the transversus with obliques, and rectus abdominis in the maximum voluntary retraction action. Both of these abilities, which represent elements in the voluntary effort of defaecation, were argued by Sikirov (2003) as being more necessary in seated (as compared to squatting) defaecation. It follows that voluntary trunk muscle control over intra-abdominal pressure, if deficient in STC children, could contribute to the diminished defaecation capacity in these children.

The STC children had a significantly greater resting anteroposterior abdominal diameter, which was not likely to be a function of a difference in the size of the STC as compared to the control group children (there was no significant difference in body mass index between the two participant groups, or in body weight as a percentile). Three possible explanations for the increased resting anteroposterior diameter in the STC group are a fuller colon, a different sitting posture, and poor postural abdominal muscle control. A fuller colon was not investigated. A different sitting posture could operate in both directions; that is poor abdominal muscle control could have augmented the more slumped posture in the STC group, or the slumped posture could have affected the abdominal muscle control.

When the voluntary contractions was examined, the STC participants demonstrated significantly reduced ability to bulge, which we and others believe is a factor in efficient defaecation (Sapsford & Hodges, 2001; Sapsford, et al., 2001). There was no statistical evidence that children with STC were different in their voluntary retraction ability. Although the ability to retract was the same in the two groups, the question remains as to whether the

STC children might retract more often during defaecation, given that it has been shown that this retraction pattern of abdominal action may lead to co-contraction of the external anal sphincter, and if used in an attempt to defaecate may in fact lead to a degree of obstructed or incomplete defaecation (Sapsford & Hodges, 2001; Sapsford, Markwell, & Richardson, 1996). Sapsford and co-workers (2001) also showed that holding the abdomen in the bulged position allows an increase in intra-abdominal pressure without an increase in external anal sphincter activity.

The study did not allow determination of whether the musculoskeletal changes are an integral part of STC, or a consequence thereof, and it is a matter of conjecture as to the extent to which this is clinically relevant in children with STC. However it points to the logic of attempting to improve the use of abdominal muscles, as well as to improve posture, during defaecation.

The reasonable suggestion that the STC participants could not bulge as well as the control subjects because their abdomen was already more-bulged in the resting position, is not supported by the analysis in all subjects (shown in Figure 4) of the ability to bulge and retract as a function of the resting anteroposterior diameter. Although challenging, more sophisticated research will be necessary to determine whether the trunk muscle deficiencies found in the present study are part of the STC syndrome, a consequence of a general malaise resulting from the STC disorder, or some other factor(s). Detailed function of pelvic floor muscles and anal sphincter muscles in children with STC also deserves investigation.

5.7.3 Joint mobility

The finding of connective tissue atrophy in megacolon by the team of Meier-Ruge, et al. (2006), and their clarification of how a fibrous net of connective tissue within the circular and longitudinal muscle of the colon is essential for peristalsis, reinforced the inclusion of trunk mobility assessment in the present study. It was also surmised that trunk mobility could interact with muscle control in determining defaecation posture and function.

We found no evidence for any difference in spinal mobility between the two groups. However, we acknowledge that there might still be some difference in connective tissue behaviour, arrangement, extensibility or stiffness. More sensitive testing may be necessary.

For example, Yazgan and colleagues (2008) have recently reported an inverse correlation between serum prolidase and generalised joint hypermobility in children. Other investigations could include skin extensibility, diastolic pressure, bone atrophy and kidney collagen degradation products as in the study of hypermobile children undertaken by Engelbert, et al. (2003).

5.7.4 Activity levels

A lack of regular sporting activity has been cited as a risk factor for constipation in children aged 7–12 years (Inan, et al., 2007), and regular exercise is often encouraged as a treatment for constipation at all ages. It might have been expected that the STC children would have been disinclined to exercise for a number of reasons: (1) general malaise associated with STC, (2) lack of energy from poor appetite and decreased calorific intake, (3) a sense of fullness and bloating, (4) chronic abdominal discomfort from slow passage of stool, (5) concerns relating to involuntary passage of stool, and (6) disinclination to reveal to others protective clothing or an appendicostomy site. Many of these issues were identified in the study of quality of life in children with STC by Clarke (2008). Also noteworthy in Clarke's study was the finding that whilst STC children scored somewhat less on the quality of life questionnaire than control children, the parents of the STC children scored their child's quality of life much lower. This suggests that these children, whilst not entirely happy, nevertheless feel they can cope and 'get on with life'. This would be in keeping with the finding in the present study of no difference in hours of exercise in the STC and control children.

The present study revealed that children with STC who exercised most (> 15 hours / week), were less involved in sedentary activities. By contrast, the control children who exercised most were also involved in a lot of hours of sedentary (TV and computer) activities. One possible explanation could be the parents, believing that physical exercise is beneficial, strongly encouraged the STC children to undertake outside-of-the-home recreation and sport; which may have left the children so tired or malaised that they were disinclined to do anything else when indoors.

We acknowledge a weakness in the activity profiling of the children in this study was failing to account for all hours of the children's waking day. The total hours of physical and sedentary activities ranged from a minimum of 5.8 hours to a maximum of 59.5 hours. Apart from School, sleeping and eating, which we assumed would occupy roughly equal amounts of physical and non-physical activity, we did not find out what else occupied each subject's day.

Whilst we do not know what else the children did, it remains a valid finding that the pattern of high and low hours of physical and sedentary activities was different in the two subject groups, and deserves further investigation. Many studies such as those by Bagley et al. (2006) and Hinkley et al. (2008), have shown that there are multiple factors with complex interactions contributing to the pattern of physical exercise and television viewing in children and adolescents; including number of siblings, mother's educational status and number of television sets in the home. Without a careful epidemiological study it may not be possible to resolve the different relations between physical exercise and sedentary activity in the STC as compared to the control subjects revealed in our study.

5.8 Conclusion

The significant inability of the STC participants to voluntarily bulge their abdomen, and their reduced ability to actively extend the trunk, suggests that children with STC may have either or both, of reduced trunk muscle strength and endurance. A limitation of this study is that it cannot differentiate whether these results are the cause or effect of STC. Alternatively these deficiencies might be caused by a problem of reduced muscle control. There was no evidence of a difference in spinal mobility between the two subject groups. There was, however, a more-flexed defaecation sitting posture and a reciprocal relationship between the usual hours of physical and sedentary activities in the children with STC. These findings have implications for defaecation training. We recommend that clinicians place greater focus on awareness and training of trunk muscles involved in defaecation and correction of sitting posture as an integral part of the management of these children.

It now remains to undertake further research in an effort to clarify the cause and consequences of these findings.

5.9 Acknowledgements

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CHAPTER 6: DISCUSSION

6.1 Summary of findings

A systematic review of the efficacy of non-pharmacological, non- surgical and non-behavioural treatments of functional chronic constipation in children confirmed that despite the need for new effective treatments for childhood constipation, there is little work published in this area. In general, the evidence for the efficacy of the identified non-pharmacological, non- surgical and non-behavioural treatments (reflexology, chiropractic, acupuncture and transcutaneous electrical stimulation) was of low quality. There was available literature discussing the use of electroacupuncture and transcutaneous electrical stimulation to influence gastrointestinal motility but none of this work was in children. It was on this basis that the randomised sham-controlled trial to investigate the use of transcutaneous interferential (IFC) current on Slow Transit Constipation (STC) in children was undertaken.

The results of the randomised sham-controlled trial found that practice-based transcutaneous electrical stimulation using IFC increased bowel motility, decreased bowel transit time, pain and soiling and improved physical quality of life in children with STC.

To investigate if home-based treatment was feasible and if similar results could be achieved with a less expensive stimulation machine, a pilot study comparing IFC and TENS was undertaken. Results from this study were inconclusive, except to demonstrate that families managed the use of both machines without difficulty and that there were trends to improvement in some symptoms. A follow-up randomised controlled trial is required to compare the effectiveness of these two modalities.

Clinical observations of children with STC noted two body types - either low body mass index with tight abdominal musculature and postural lumbar flexion and thoracic flexion, or high body mass index with low tone abdominal musculature and postural lumbar flexion and thoracic flexion. A standardised musculoskeletal assessment was undertaken to investigate this further. This study showed no evidence of a difference in spinal mobility, Marfenoid characteristics, body mass index and body weight between children with STC and children with typical development. However, the results suggested that children with STC may have either reduced trunk muscle strength or muscle endurance, or both, or these deficiencies might be caused by a problem of reduced muscle control. There was a more-flexed defaecation sitting posture in the children with STC. Whether these are a cause or an effect of defaecation difficulty is not known.

6.2 Clinical implications

The overriding implication of this research is that the management of children with severe and chronic constipation may be best addressed by a team of health practitioners offering physical therapies as well as psychological and medical interventions. The treatment with IFC was additional to any toileting programme or laxative regime the children were currently undertaking, and therefore must be regarded as adjunctive therapy. This is the case when electrical stimulation is used in other forms of rehabilitation. For example if electrical stimulation is used to inhibit detrusor overactivity in the treatment of urinary urge incontinence, concurrent voiding regimes to re-educate sensory stimuli and relaxed voiding are part of treatment (Lordelo, Soares, Maclel, Macedo, & Barroso, 2009).

The children had toileting programmes or laxative regimes over the previous two years with no effect and their bowel transit studies had not changed prior to IFC. It has been shown that nuclear transit studies are reproducible in assessing slow colonic transit in children with treatment-resistant STC and had been demonstrated that conventional medical treatment over many years had no effect on underlying colonic motility if symptoms persisted (Clarke, et al., 2009). It was concluded that it was IFC that had altered the colonic motility, so it follows that IFC provides an accessible, comfortable new additional treatment option for children with STC with no known adverse side-effects.

It was necessary to maintain toileting regimes until the children developed some awareness of the need to defaecate. We observed that children slowly developed the urge to defaecate, which initially they seemed not to recognise. In fact some children commented they had never felt such an urge before. As we understood this, it was pointed out to them that any small change in feeling (be it abdominal or rectal) may represent peristalsis and they should respond accordingly. As the ability to perceive the need to defaecate is so important an attempt was made to develop a measure of rectal perception – a visual analogue scale (see below).

In the last week have you had any feeling in your bottom of needing to do a poo?

0 I____I 10
none strong and definite feeling to poo

Some children found this useful and others did not, possibly because the time frame (in the last week), was too long for them to remember a sensation. This needs further thought and development. Focussing on the child's perceptual abilities in relation to defaecation is an area of treatment that to date has not been addressed outside diagnostic testing of sensation undertaken with ano-rectal manometry. But as with the re-education of response to bladder sensations in the treatment of bladder overactivity, it is sensible to incorporate this into treatment.

More distension treatment would be expected to be more effective in re-education of perceptual abilities. Eleven children in the RCT who did not respond or relapsed were treated with daily stimulation at home (Ismail, et al., 2009). Nine of the eleven children had increased defaecation and four had decreased soiling. The increase in total episodes of defaecation per week was significant ($p<0.01$) and the decrease in soiling was non-significant ($p=0.1$). The choice of three times per week was originally made according to the families' ability to attend a physiotherapy practice. In the treatment of refractory bladder overactivity in children, neuromodulation is more commonly done with TENS over the third sacral foramina and treatment intensity varies. Some children respond to 20 minutes 3 times per week (Lordelo, et al., 2009) and others for a period of two hours daily (Hagstroem, Mahler, Madsen, Djurhuus, & Rittig, 2009). The optimum duration and length of stimulation is not known, neither are the indications for those who will respond better, but for children who are non-responsive to lesser amounts of duration and frequency of treatment, there is an argument for increasing both these parameters.

The ideal mechanics of defaecation are an upright and forward leaning sitting position to facilitate defaecation by lengthening the anal aperture and widening the ano-rectal angle. Ideally, if sitting posture is correct and faecal consistency normal, expulsion occurs, in the main, by rectal propulsion once sphincter release has occurred. If necessary, transversus abdominis is the first muscle recruited to generate increased intra-abdominal pressure, followed by the internal and external oblique muscles, the diaphragm, and to a lesser extent rectus abdominis. If action of these abdominal muscles is maintained with an open glottis then spinal stability is also enhanced. In Chapter 5 it was concluded that the STC participants had a less-than-optimum posture during defaecation. This finding points to the logic of attempting to improve defaecation posture in STC children.

Clinically, one typical straining pattern in children during defaecation is flexed lumbar spine, breath-holding at the peak of inspiration and in-drawing of rectus abdominis. This leads to anal closure. It is the pattern of a Valsalva manoeuvre in which the pelvic floor muscles and sphincters are recruited to maintain continence. Once the sensation this engenders is pointed out and compared to the sensation of the correct position and action, many children understand it immediately. Others take more time and practice as they have limited ability to change their lumbar spine posture and decreased voluntary trunk muscle control over intra-abdominal pressure. Awareness and training of trunk muscles involved in defaecation and correction of sitting posture are an integral part of the management of these children.

6.3 Mode of action of electrical stimulation with interferential current.

The mechanism of the effect is, at present, unknown. Neuromodulation of the bowel provides a reasonable explanation for the effect of IFC on bowel motility. Neuromodulation is the term used to cover an induced change in "neural traffic" over time. Bowel actions were rarely stimulated by treatment immediately. Rather, a more gradual improvement over successive days and weeks occurred. Trophic effects as the result of application of current have been shown and include vasomotor and secretory responses (Robertson, Low, Reed, & Ward, 2006). Such effects in the bowel could be explained by sympathetic inhibition and also lead to improved bowel functioning over time. Neuromodulation of the bladder with electrical current is a well-established treatment in adults and children (Bergmans, Yamanishi, & Wilson, 2005; Hagstroem, et al., 2009), and is proposed to act centrally by re-balancing excitatory and inhibitory information and returning the neural drive towards a more normal status. In the treatment of detrusor over-activity this is done less invasively with transcutaneous electrodes. It is likely that changes are mediated by supraspinal as well as spinal pathways, as evidenced by work showing EEG activity in the post-central gyrus during S3 stimulation (Braun, et al., 2002).

Electrical current stimulates nerves, and there are several possibilities as to which nerves were affected. Modulated IFC will spread in many directions according to the tissue arrangement because of differences in their impedance, and unless the orientation of nerve fibres is optimal, stimulus modulation may be partial (Ward, 2009). However the electrode configuration in the RCT “makes any 'interferential' or 'depth efficient' stimulation out of the question as the trunk would behave like a ‘tube of isotonic fluid’ so current would not concentrate between the electrodes. The major effects would be produced immediately under the electrodes, and the effect of kHz frequency stimulation would be bombardment of neurons close to the electrodes with essentially continuous AC which would result in autonomic (mostly sensory) fibres being stimulated at close to their maximum firing frequencies. So the likely explanation would seem to be “autonomic reflex activation” (Ward, 2010). When applying electrical current, larger diameter nerves will selectively be stimulated before smaller diameter nerves. The intensity of stimulation in the RCT was comfortable; we did not stimulate A-δ or C fibres, but more likely superficial A-α and A-β fibres. Again this points to the effect on bowel motility being a reflex effect via somatovisceral reflex activity explained by reciprocal depolarisation of visceral and somatic afferents converging on lamina 5 of the dorsal horn of the spinal cord, resulting in central relay of information (Camilleri, Malageladam, Kao, & Zimnmeister, 1984).

It is feasible that the effect of IFC on bowel motility was caused by altered levels, or altered balance of levels of inhibitory and excitatory neurotransmitters. Electrical stimulation has been shown to change levels of neurotransmitters. Changes in levels of substance P in the rectal mucosa have been demonstrated following both 14 and 90 days of continuous sacral nerve stimulation (Gooneratne, et al., 2008). In using electrostimulation to treat bladder overactivity, beta-adrenergic activity is enhanced (facilitating bladder vault relaxation), cholinergic activity reduced, and changes occur in the concentration of selected smooth muscle relaxants (vasointestinal peptide and serotonin). Other neurotransmitter substances that have been shown to change in availability include GABA, acetylcholine, dopamine, serotonin, vasopressin, and nitric oxide (Bower & Yeung, 2004). Electric current is also known to stimulate the release of endorphins and encephalins in the cerebrospinal fluid, and raised opioid levels following stimulation have been reported to be inhibitory to detrusor overactivity (Bower & Yeung, 2004).

6.3.1 Activation of extrinsic nerves

Bowel motility is modulated by both intrinsic (enteric nervous system) and extrinsic autonomic nerves, that is parasympathetic and sympathetic nerves. Extrinsic nerves coordinate perception, responses to meals and defaecation, and central connections are also essential for coordinated smooth muscle contraction in the bowel. The potential for stimulation of each will be considered in turn.

Sympathetic effect

Electrodes were placed over T10-L2 paraspinally. The T5-12 spinal cord provides sympathetics to the colon, while L1–3 provides sympathetics to the rectum. An effect on sympathetic nerves was possible. Sympathetic pathways originate in the thoraco-lumbar spinal cord with sympathetic "preganglionic "neurons largely in the intermediolateral cell column. These project to sympathetic ganglia where they synapse onto sympathetic "post-ganglionic neurons" which then innervate the gut wall. The major targets of sympathetic post-ganglionic neurons include the myenteric and submucosal ganglia, mesenteric and enteric blood vessels, the gastrointestinal mucosa and, to a lesser extent, the smooth muscle ("muscularis externa") of the gut wall. The major effects of sympathetic neurons in the gut wall are to cause inhibition of enteric neuronal transmission, mostly by presynaptic inhibition via alpha adrenoceptors, however they also cause vasoconstriction and changes in secretion and muscle tone. If an effect on thoracolumbar sympathetic nerves occurred, either directly or by activated reflexes, the frequency of stimulation must have inhibited these nerves, that is, the inhibitor was inhibited. However there is little information available on the electrical parameters needed to stimulate or inhibit sympathetic nerves.

Parasympathetic effect

It is unlikely that direct stimulation of parasympathetic nerves occurred. The vagus nerve (cranial X) provides the gut with parasympathetic fibres down to and including the transverse colon. Sacral parasympathetics (S2-S4) and their associated visceral afferents supply the descending colon, sigmoid and rectum. A potential reflex excitatory effect on sacral or vagal nerve fibres would lead to stimulation of rectum and descending colon, or ascending and transverse colons respectively.

6.3.2 Activation of the enteric nervous system

What else was activated by reflex activity or the “trickle down” effect is a matter of conjecture. The enteric nerves and the interstitial cell of Cajal (ICCs) are both influenced by autonomic activity, and in this way may have been affected.

The enteric nervous system (ENS) is a relatively self-contained nervous system with a complex integration of nerve cells and ganglia. The enteric nerve cell bodies and glial cells are contained within ganglia networks –the one between the circular and longitudinal muscle being the myenteric (Auerbach) plexus, the submucosal plexus exists between the mucosal cells and the circular muscle. A third group of enteric nerves is found within the circular and longitudinal. These work in an integrated way to monitor and manipulate the muscular contractile state of the gut wall, the secretary activity of the mucous glands, blood flow and the contents of the lumen.

The interstitial cells of Cajal (ICCs) are unique variants of smooth muscle cells derived, as are the smooth muscle cells, from the gut mesenchyme. They also are influenced by autonomic activity. They are concentrated on either side of the circular muscle layer in close proximity to the myenteric and submucosal enteric networks, but some can be found within the muscular layers. ICCs are pacemakers for peristaltic gut contractions. Although smooth muscle can contract in direct response to mechanical, hormonal and chemical stimuli, such contractions are not large in magnitude, regular in timing, or effective in mixing and propelling gut contents. Motility of the gut depends on the ICCs and the ENS. Dysfunctional enteric nervous system, decreased levels of substance P, decreased numbers of Interstitial cells of Cajal (ICC) and connective tissue disorders have all been implicated in STC (Hutson, et al., 2004). In studies on rats it has been shown that induced partial colonic obstruction leads to a downgrading of ICCs distal to the obstruction, but no cell death. When the obstruction is relieved, the ICCs recover (Sanders, Ordog, & Ward, 2002). In healthy humans gut ICCs are in a continual state of replacement (Gibbons, et al., 2009). Considering there appears to be plasticity in the ICCs the potential exists for electrical current which causes changes in neural activity to have ongoing effects.

6.4 Strengths and weaknesses of this body of work

6.4.1 Strengths

The work in this thesis related to a specific group of children with constipation - they had STC that had been unresponsive to at least two years of treatment. There were well-defined inclusions and exclusion criteria, which meant that the condition was objectively demonstrated by transit studies and also documentation was available that previous treatment had not been successful and other diseases or conditions causing constipation were excluded. Children with constipation are not a homogenous group. Symptoms may be similar for example, with STC and functional faecal retention, but interventions can only be evaluated if the participants have a similar diagnosis. In all but one study identified in the literature review (Chapter 2) this was not so.

Subjective and objective outcome measures were used. In the RCT, care was taken to engage the children and parents or care-givers in achieving a consistent record in the bowel diary, which was the subjective outcome measure. The trial was named 'Tic Toc' (Transcutaneous interferential current to overcome constipation). Diaries were formatted with different colour pages for different stages of the trial and interspersed at random were motivational cartoons to keep completing the diary. Baseline recording of bowel function by bowel diary for one month was completed and continued throughout the study. Bowel diaries were accompanied by specific instructions for their use and families were individually taught how to do this. (see Appendices E, G & H) At each contact visit each page was checked and any lack of clarity resolved with the family at the time. All bowel diary data were entered into the database by two people and cross-checked.

In the studies identified in Chapter 2, the lack of measures used to evaluate the wellbeing of children, and the lack of any objective measure of bowel function before and after the intervention were seen as weaknesses. As no quality of life measure for children with bowel dysfunction existed, generic validated quality of life questionnaires to measure both parent and child answers were used. Bowel transit studies were used as an objective before and after outcome measure, and the same protocol was followed by the Medical Imaging Department.

By repeating the outcome measures, including the transit studies, two months after the cessation of the intervention, it was considered that any potential transitory response caused by attending a physiotherapist weekly would have passed. This time-frame also gave an indication of the ‘carry-over’ effect of stimulation.

Bias was minimised in the following ways. Patients and all trial staff, except for the treating physiotherapist, were blinded to treatment. Randomisation was known only to the treating physiotherapist and the code was broken after data entry and analysis. Children and families were told that two levels of stimulation were being trialled and that with either level there may or may not be a sensation of stimulation – this wording was consistent with all staff, and some children reported sensation with the sham machine. Physiotherapists often experience this with patients reporting warmth or tingling before a machine is turned on. Treating physiotherapists were individually instructed by trial staff as to their role and consistent wording and behaviour to be used with children and families whichever machine was being used - for example they returned to adjust intensity on the sham machine as they would for the real one, and inspected the skin for any redness after sham stimulation also. Their behaviour was the same for each machine. They did not give advice or enter into conversation about the treatment except to encourage diary completion, so results would not be contaminated by any other interventions.

In the musculo-skeletal study, the conclusions were able to be drawn because of the comparison to an age- and gender- matched group without bowel dysfunction. There were more boys in the control group as there were in the STC group. Children who participated in the control group were not friends or relatives of the STC children as this may have led to bias. All questions, measurements and photos were taken by one therapist, and all analysis done by another therapist using sophisticated computer measurement tools, so ensuring consistency. As a result of basic research into the reliability of obtaining linear and angular measures by photography and computer analysis by the therapist who did the analysis, there was confidence in the reliability of this method, although validity was not established (Stillman, 2000). In the abdominal bulging research, for example, the measurements were often relative (percentage difference) measures of distances from 'adjacent photographs' of the same child with constant camera and stool and distance variables between photos. So any error, for example from a tilted camera, would be relatively insignificant but was minimised by the camera being on a tripod.

6.4.2 Weaknesses

There is no validated quality of life measure specifically designed for bowel dysfunction in children. There is one for bladder dysfunction in the paediatric population called PinQ (Bower, Sit, Bluyssen, Wong, & Yeung, 2006; Bower, Wong, & Yeung, 2006) (Appendix L), which consists of 20 items answered by the child from ages 6 years and older.

In the randomised sham-controlled trial, we used the Pediatric Quality of Life Inventory (PedsQL) (Varni & Kurtin, 2001; Varni, Seid, & Rode, 1999; Varni, Seid, Knight, Uzark, & Szer, 2002). (see Appendices C & D) Comparing the questions asked in this generic quality of life tool to the questions asked by PinQ regarding the impact of bladder problems, it can be seen that a disease-specific quality of life measurement tool would be advantageous and give more detailed information about the impact of constipation and soiling on the child by measuring more relevant items. For example, no difference in the general activity level of children with STC compared to the control group was identified. However in the RCT, one of the outcomes was a significant improvement in the physical quality of life. The PedsQL physical domain included questions regarding walking more than one block, running, participating in sports activity or exercise, lifting something heavy, taking a bath or shower by yourself, doing chores around the house , having hurts or aches and having a low energy level, that is, there was more to the physical domain of PedsQL than exercise or activity. It was observed that walking more than a block, lifting, doing chores and showering did not present a challenge to the children with STC. A significant decrease in abdominal pain was demonstrated in the RCT and it was concluded that this may have altered the answers to some of the other questions such as energy levels and hurts and aches. A disease-specific tool should make this clearer.

The role of pelvic floor musculature was not assessed in this study. Lack of voluntary control, awareness of contraction versus relaxation may impact on complete rectal evacuation. Pelvic floor laxity or weakness could contribute to lack of rectal funnelling during defaecation, or deficiencies in rectal perception. It is generally agreed that some degree of rectal perception originates from pelvic floor muscle stretching or pressure. Pelvic floor muscle integrity is also necessary to efficiently generate increases in intra-abdominal pressure. The potential for pelvic floor muscle retraining applies to two conditions broadly speaking. One is pelvic floor dyssnergia, which defines an inability to relax or an active contraction during defaecation (Benninga, et al., 2005) – relaxation training would be the aim. The other is pelvic floor muscle weakness and strength training would be the treatment. Children with STC may also have pelvic floor dyssynergia (Treepongkaruna, et al., 2001). The long-term benefits of biofeedback either with perineal EMG or rectal balloon training to treat pelvic floor dyssynergia have not been demonstrated (Loening-Baucke, 1995, 1996; Sunic-Omejc, et al., 2002). Studies using biofeedback have not assessed the function of the pelvic floor muscles, such as strength, endurance, proprioceptive awareness, ability to contact and relax on request, or prescribed exercise accordingly. These are routinely assessed in the treatment of adult continence problems and give insight into the role of pelvic floor muscle/sphincter dysfunction in defaecation difficulty and hence treatment aims. For example, in the treatment of Descending Perineal Syndrome, characterised by lack of rectal funnelling during defaecation, loss of rectal sensation, chronic rectal distension and incomplete emptying and consequent faecal incontinence, treatment is pelvic floor muscle retraining especially in regard to endurance training, and re-educating of defaecation dynamics. Whether children would respond to a similar intervention is not known, but assessment of muscle function is needed first. It has been shown that pelvic floor muscle assessment in children is possible by the use of transabdominal ultrasound (Bower, Chase, & Stillman, 2006). This method and the use of electromyography, could be used to research and clarify the role, if any, of pelvic floor muscle function in children with STC.

When researching the activity levels of children, we looked at the average hours per week of physical activity (e.g. walking, cycling, bike-riding and sport) and sedentary activity (ie. television viewing and computer activities) outside of school time. We did not thoroughly investigate the type of activity the children undertook. We cannot comment on whether it was a solitary pass-time like bike riding or a team sport. It may be that due to abdominal discomfort, or concerns about soiling or changing clothes, children with STC chose exercise that allowed them to participate in their own time-frame and comfort zone. This could perhaps also explain an improvement in physical quality of life in the RCT if following treatment the children were more able to participate in group or overnight activity. This sort of participation has implications for overall health, socialisation and general enjoyment, and further research is warranted.

There were some limitations with statistical analysis. Lack of stratification according to severity of symptoms In Chapter 3 lead to an inability to meaningfully compare the two groups post-treatment. Changing from an office-based intervention to home use of both TENS and portable IFC lead to a lack of compliance which affected data collection. Incomplete bowel diaries and missing QoL data limited statistical analysis as reported in Chapter 4. Had this been foreseen, then the inclusion of prompted weekly reporting in the TENS trial protocol could have been used to improve adherence and compliance.

6.5 Suggestions for further research

Following the work presented in this thesis it is suggested that the following areas require more research. To determine the optimal electrical parameters for transcutaneous electrical stimulation to treat STC in children, frequency of current, length and duration of treatment, type and intensity of current and whether the effect can be enhanced by alternative electrode placement need to be investigated. Thoracic placement of electrodes has the potential to inhibit sympathetic activity and sacral placement has the potential to enhance rectal motility and sensation. Whether other forms of constipation such as functional faecal retention can also be helped by transcutaneous electrical stimulation and whether this can be done more effectively by sacral placement of electrodes needs investigation.

Undertaking a cost analysis of home-based IFC and ‘current management’ vs ‘current management’ alone would provide information regarding the cost-benefits of using electrical stimulation to the health system. Another cost consideration as to whether electrical stimulation can be offered more cheaply requires repetition of the study comparing IFC and TENS to determine if the same effect can be achieved by a cheaper machine. There are also implications for access and intensity of treatment for children in this country who live far from treatment centres, as well as time and cost implications.

Future studies would benefit by a disease-specific quality of life questionnaire for children with STC, and a non-invasive measure of rectal perception. Generic quality of life tools often lack the subtle qualities, or responsiveness, required to detect “change”. At the time of this research there was no psychometrically tested quality of life tool for children with bowel dysfunction. Rectal perception is an important component of rectal evacuation and faecal continence and children are able to report it. There is no validated non-invasive tool to measure it before and after interventions.

To assess the function of pelvic floor muscles in children with STC using transabdominal ultrasound and electromyography would give insight into potential muscle retraining programmes for children with STC. As a result of the findings in Chapter 5, the next step is to develop an age-appropriate exercise regime to improve trunk muscle strength, endurance and control, and evaluate whether this has an effect on defaecation efficiency in children with STC, using measures of rectal perception, rectal diameter on transabdominal ultrasound, soiling and defaecation frequency. Studying the type of activity, hobbies or exercise in which children with STC choose to participate, has implications for improving the children's quality of life.

The development of a composite outcome measure would improve the measurement of effect of the interventions and potentially include quality of life, rectal perception, medication use as well as bowel diary measures.

6.6 Conclusion

The results of this research confirm that the management of children with severe constipation and associated faecal incontinence is far from perfect and that novel treatments are needed. It also confirms that physiotherapy and electrostimulation have a role in the treatment of children with severe constipation and suggests that, as in adult management, a multi-disciplinary team of health practitioners is necessary to provide care for children with a chronic condition that involves an interplay of autonomic (gut motility) and somatic and cognitive (pelvic floor control, perceptual ability) as well as behavioural and psychosocial factors. It is suggested that if each of these aspects is addressed, treatment success is more likely. The aim is to improve the children's quality of life, and to impact on the children with constipation who carry it into adult life and are predisposed not only to further bowel dysfunction, but also to lower urinary tract dysfunction and both faecal and urinary incontinence, pelvic organ prolapse and pelvic pain.

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APPENDIX A: Data Extraction Form

Data Extraction Form

The efficacy of non-pharmacological, non-surgical and non-behavioural treatments of functional chronic constipation in children

Reviewer: ____________________________**Date of extraction:** / /

Included ☐ **Excluded** ☐

…………………………………………………..........

Full reference details (author, title, source, country of origin of study):
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Study Objective:
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....

Study design:
....
....
....

Subject details:

Inclusion criteria:
....
....

Exclusion criteria:
....
....

Recruitment procedures used:
....

Control Subject number:……………………………………………..	Control...................................
Sex:………………………..

Control Age (mean and range): ....

Subject number experimental:……………Experimental Sex: ....
Experimental Age (mean and range): ....

Group characteristics (e.g. pathology, demographics)
Experimental group:
....
....
....

Control group:
....
....
....

Description of Intervention (content e.g, massage, manipulation, electrical therapy)
....
....

Frequency:
....
....

Duration of treatment program:
....

Setting for intervention (environment):
....

Outcome measures used (at baseline and follow-up):-
....
....

Were the tools used to measure the intervention valid and reliable? How was this demonstrated?
....
....
....

Results:

....
....
....

Additional comments (e.g. adverse events):

....
....

APPENDIX B: Royal Children's Hospital Human Research Ethics Committee Approval (23040A)

Royal Children's Hospital, Melbourne

Flemington Road, Parkville
Victoria, Australia, 3052

Telephone (03) 9345 5522
ISD (+613) 9345 5522
Facsimile (03) 9345 5789

ETHICS IN HUMAN RESEARCH COMMITTEE APPROVAL

EHRC REF. No:	**23040 A**
PROJECT TITLE:	Colonic manometry and transcutaneous stimulation (using interferential therapy) in Slow Transit Constipation. TGA No. L 27572
Documents approved:	P/GIS and Consent, v1 dated 17 Mar 2003. PIS and Consent, v1 dated 17 Mar 2003. Bottom Line Newsletter, v1 June 23 2003.
Approved Protocol:	Protocol, v2 dated 28 May 2003.
INVESTIGATOR(S):	B Southwell, J Hutson, S Gibb, A Catto-Smith, J Chase, V Robertson, S King, J Sutcliffe

DATE OF NEW APPROVAL: **24 June 2003.**

DURATION: 36 months

SIGNED: 27/6/03

COMMITTEE REPRESENTATIVE

APPROVED SUBJECT TO THE FOLLOWING CONDITIONS:

ALL PROJECTS

1. Any proposed change in protocol and the reasons for that change, together with an indication of ethical implications (if any), must be submitted to the Ethics in Human Research Committee for approval.
2. The Principal Investigator must notify the Secretary of the Ethics in Human Research Committee of:
   - Actual starting date of project.
   - Any adverse effects of the study on participants and steps taken to deal with them.
   - Any unforeseen events.
3. A progress report <u>must</u> be submitted annually and at the conclusion of the project, with special emphasis on ethical matters.

DRUG TRIALS

4. The investigators must maintain all records relating to the study for a period of 23 years.
5. The investigator(s) must report to the Sponsor <u>and</u> the Ethics in Human Research Committee within 24 hours of becoming aware of any serious adverse event experienced by any subject during the trial.
6. The investigators must ensure that all externally sponsored Clinical Drug Studies have insurance coverage that is current for the entirety of the study.

APPENDIX C: PedsQL - Pediatric Quality of Life Inventory – Version 4 - CHILD REPORT (ages 8-12)

ID# ______________________________

Date:_________________________

PedsQL ™

Pediatric Quality of Life Inventory

Version 4.0

CHILD REPORT (ages **8-12**)

DIRECTIONS

On the following page is a list of things that might be a problem for you. Please tell us **how much of a problem** each one has been for you during the **past ONE month** by circling:

0 if it is **never** a problem
1 if it is **almost never** a problem
2 if it is **sometimes** a problem
3 if it is **often** a problem
4 if it is **almost always** a problem

There are no right or wrong answers.

If you do not understand a question, please ask for help.

In the past **ONE month**, how much of a **problem** has this been for you

About My Health and Activities ***(PROBLEMS WITH…)***	Never	Almost Never	Some-times	Often	Almost Always
1. It is hard for me to walk more than one block	0	1	2	3	4
2. It is hard for me to run	0	1	2	3	4
3. It is hard for me to do sports activity or exercise	0	1	2	3	4
4. It is hard for me to lift something heavy	0	1	2	3	4
5. It is hard for me to take a bath or shower by	0	1	2	3	4
6. It is hard for me to do chores around the house	0	1	2	3	4
7. I hurt or ache	0	1	2	3	4
8. I have low energy	0	1	2	3	4

About My Feelings ***(PROBLEMS WITH…)***	Never	Almost Never	Some-times	Often	Almost Always
1. I feel afraid or scared	0	1	2	3	4
2. I feel sad or blue	0	1	2	3	4
3. I feel angry	0	1	2	3	4
4. I have trouble sleeping	0	1	2	3	4
5. I worry about what will happen to me	0	1	2	3	4

How I Get Along with Others ***(PROBLEMS WITH…)***	Never	Almost Never	Some-times	Often	Almost Always
1. I have trouble getting along with other kids	0	1	2	3	4
2. Other kids do not want to be my friend	0	1	2	3	4
3. Other kids tease me	0	1	2	3	4
4. I cannot do things that other kids my age can do	0	1	2	3	4
5. It is hard to keep up when I play with other kids	0	1	2	3	4

About School ***(PROBLEMS WITH…)***	Never	Almost Never	Some-times	Often	Almost Always
1. It is hard to pay attention in class	0	1	2	3	4
2. I forget things	0	1	2	3	4
3. I have trouble keeping up with my schoolwork	0	1	2	3	4
4. I miss school because of not feeling well	0	1	2	3	4
5. I miss school to go to the doctor or hospital	0	1	2	3	4

APPENDIX D: PedsQL - Pediatric Quality of Life Inventory-Version 4 - PARENT REPORT (ages 8-12)

ID# ___________________________

Date:___________________________

PedsQL ™

Pediatric Quality of Life Inventory

Version 4.0

PARENT REPORT for **CHILDREN** (ages **8-12**)

DIRECTIONS

On the following page is a list of things that might be a problem for **your child**. Please tell us **how much of a problem** each one has been for **your child** during the **past ONE month** by circling:

0 if it is **never** a problem
1 if it is **almost never** a problem
2 if it is **sometimes** a problem
3 if it is **often** a problem
4 if it is **almost always** a problem

There are no right or wrong answers.

If you do not understand a question, please ask for help.

In the past **ONE month,** how much of a **problem** has your child had with

Physical Functioning (*PROBLEMS WITH…*)	Never	Almost Never	Some-times	Often	Almost Always
1. Walking more than one block	0	1	2	3	4
2. Running	0	1	2	3	4
3. Participating in sports activity or exercise	0	1	2	3	4
4. Lifting something heavy	0	1	2	3	4
5. Taking a bath or shower by him or herself	0	1	2	3	4
6. Doing chores around the house	0	1	2	3	4
7. Having hurts or aches	0	1	2	3	4
8. Low energy level	0	1	2	3	4

Emotional Functioning (*PROBLEMS WITH…*)	Never	Almost Never	Some-times	Often	Almost Always
1. Feeling afraid or scared	0	1	2	3	4
2. Feeling sad or blue	0	1	2	3	4
3. Feeling angry	0	1	2	3	4
4. Trouble sleeping	0	1	2	3	4
5. Worrying about what will happen to him or her	0	1	2	3	4

SOCIAL FUNCTIONING (*problems with…*)	Never	Almost Never	Some-times	Often	Almost Always
1. Getting along with other children	0	1	2	3	4
2. Other kids not wanting to be his or her friend	0	1	2	3	4
3. Getting teased by other children	0	1	2	3	4
4. Not able to do things that other children his or Her age can do	0	1	2	3	4
5. Keeping up when playing with other children	0	1	2	3	4

SCHOOL FUNCTIONING (*problems with…*)	Never	Almost Never	Some-times	Often	Almost Always
1. Paying attention in class	0	1	2	3	4
2. Forgetting things	0	1	2	3	4
3. Keeping up with schoolwork	0	1	2	3	4
4. Missing school because of not feeling well	0	1	2	3	4
5. Missing school to go to the doctor or hospital	0	1	2	3	4

APPENDIX E: Instructions for completing the Bowel Diary

WELCOME TO THE TIC TOC TRIAL

………..and thank you for being part of it. We hope that you enjoy your involvement and we look forward to getting to know you better.

If at any time you have any questions or problems in regard to the trial, do not hesitate to phone us.

Janet Chase:	Ph: 9345 6458 Wednesday and Thursday or 9345 5805
Susie Gibb:	Ph: Paging service 93871000

On the next page you will find an explanation of how to fill in you bowel diary. You need to do this every day throughout the trial, so this will take a lot of commitment and hard work on your part, even though it should only take 1-2 minutes per day to do.

Below is a summary of how the trial works. This is also explained in The Participant Information Statement that you have already been given.

Initial assessment involves a bowel transit study (if you haven't already had one), and a check-up by Susie Gibb and a look at your back and tummy muscles and posture by Janet Chase.

Treatment occurs in 5 steps
Step 1 - 4 weeks of bowel stimulation using one form of current
Step 2 - 2 months of bowel diary
Step 3 - 4 weeks of bowel stimulation with the other form of current
Step 4 - 2 months of bowel diary
Step 5 - We contact you 3,6 and 12 months after therapy to see how you are doing.

INSTRUCTIONS FOR COMPLETING THE BOWEL DIARY

In this folder you should find a copy of the Bristol Stool Scale and some of the diary pages that are colour-coded according to the stage in the trial in which you are using them – blue for pre-treatment, red for the first 4 weeks of electrical stimulation, yellow for the following 2 months, purple for the second course of electrical stimulation and green thereafter. The rest we will give you as you go along.

1 The diary ***must be*** filled in each night before you go to bed, so you can remember what happened that day.

2 Make sure that ***each*** day has a date (day/month/year) and your code name is on it. This is the name you can choose so that your real name does not appear on any paperwork.

3 Under the column headed ***"Bowel action and type"***

- put a tick (√) for each bowel action you have.
- the tick goes in the 'sit' column if it happened as the result of going to the toilet to sit without any feeling of needing to poo.
- the tick goes in the 'spontaneous' column, if you went to the toilet because you had a feeling that you needed to poo.
- 'type' refers to the number that best describes the type of poo on the Bristol Stool Scale.

4 Under the column headed ***"Soiling"***

- put an 's' for each episode of soiling during the day.
- the 's' goes in the 'stain' column if the soiling was just a stain on the underwear.
- the 's' goes in the 'scrape' column if poo had to be scraped off before the underwear could be washed.

5 The column headed ***"Tablets, medicines, suppositories, enemas, washouts"*** is where you record the medicines etc.you had that day, and whether you had a bowel washout – just write "w.o." if you did.

6 The column headed ***"Physio today?"*** is to record the days that you have electrical stimulation for your bowel.

7 The next column is to record whether you have ***"Tummy pain"*** or not on each particular day.

BOWEL DIARY SHEET	**YOUR CODE NAME:**

Date started / /	*Bowel action and type*		*Soiling*		*Tablets* Medicines Suppositories Enemas Washouts	*Physio today?*	*Tummy pain today?*	*Comments*
	Sit	Spontan -eous	Stain	Scrape		Yes/no	Yes/no	
MONDAY Date								
TUESDAY Date								
WEDNESDAY Date								
THURSDAY Date								
FRIDAY Date								
SATURDAY Date								
SUNDAY Date								

Remember √ = bowel action in toilet
S = episode of soiling
type = choose a number from the Bristol Stool Scale
w.o. = washout

APPENDIX F: Royal Children's Hospital Human Research Ethics Committee Approval (26173A)

The Royal Children's Hospital, Melbourne

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RCH HUMAN RESEARCH ETHICS COMMITTEE APPROVAL

HREC REF. No:	**26173 A**
PROJECT TITLE:	A pilot study investigating using transcutaneous electrical nerve stimulation (TENS) for the treatment of slow transit constipation.
Documents approved:	P/GIS & Consent v5 dated 22 March 2007, PIS & Consent v5 dated 22 March 2007, Recruitment flyer v3 dated 17 Jan 2007, Bowel Dysfunction Assessment Demographics v5 dated 22 Mar 2007, Medical Assessment Data Sheet v3 dated 17 Jan 2007, PedsQL validated q'res (child,teen & parent), Visual Analogue Scale v3 dated 17 Jan 2007, Bowel Diary v3 dated 17 Jan 2007, How to use your TENS machine v3 dated 17 Jan 2007. Pro -Tens Operation Manual printed version.
Approved Protocol:	Protocol v3 dated 17 Jan 2007
INVESTIGATOR(S):	B Southwell c.c. M Clarke, J Hutson, S Gibb, J Chase, V Robertson, M Clarke, C Cheow, D Reilly

DATE OF ORIGINAL APPROVAL:	**29 March 2007**
DURATION:	36 Months
DATE OF APPROVAL EXPIRY:	29 March 2010

SIGNED: 30/3/2007

COMMITTEE REPRESENTATIVE DATE

APPROVED SUBJECT TO THE FOLLOWING CONDITIONS:

ALL PROJECTS

1. Any proposed change in protocol or any approved documents or the addition of any documents (including flyers, brochures, advertising material etc) and the reasons for that change or addition, together with an indication of ethical implications (if any), must be submitted to the Human Research Ethics Committee for Approval prior to implementation.
2. The Principal Investigator must notify the Secretary of the Human Research Ethics Committee of:
   - Any adverse effects of the study on participants and steps taken to deal with them.
   - Any unforeseen events.
   - Investigators withdrawing from or joining the project.
3. A progress report must be submitted annually and at the conclusion of the project, with special emphasis on ethical matters.
4. All research information collected whilst individual participants are children must be kept until the individual turns 25 (i.e. 7 years after their 18th birthday).

Please note that it is the investigators responsibility to ensure that the RCH HREC Approval remains current for the entire duration of the project. Investigators undertaking projects without current HREC approval risk their indemnity, funding and publication rights.

DRUG/DEVICE TRIALS

5. The investigator(s) must report to the Sponsor and the Human Research Ethics Committee within 24 hours of becoming aware of any serious adverse event experienced by any subject during the trial.
6. The investigators must ensure that all externally sponsored Clinical Drug Studies have insurance coverage that is current for the duration of the study.

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APPENDIX G: Instructions for completing the Bowel Diary- TENS Trial

<u>WELCOME TO THE TIC TOC TENS TRIAL</u>

………..and thank you for being part of it. We hope that you enjoy your involvement and we look forward to getting to know you better.

If at any time you have any questions or problems in regard to the trial, do not hesitate to phone us.

Janet Chase:	Ph: 9345 6458 Wednesday and Thursday or 9345 5805
Susie Gibb:	Ph: Paging service 93871000

On the next page you will find an explanation of how to fill in you bowel diary. You need to do this every day throughout the trial, so this will take a lot of <u>commitment and hard work</u> on your part, even though it should only take 1-2 minutes per day to do.

Below is a summary of how the trial works. This is also explained in The Participant Information Statement that you have already been given.

<u>Initial assessment</u> involves a bowel transit study (if you haven't already had one), and a check-up by Susie Gibb and a look at your back and tummy muscles and posture by Janet Chase.

<u>Treatment occurs in 4 steps</u>
Step 1 - 4 weeks of bowel diary
Step 2 – 2 months of TENS and bowel diary (usually a visit after 4 weeks of this)
Step 3 – 8 weeks of bowel diary
Step 4 – visit to Susie Gibb and Janet Chase at the end of 8 weeks

INSTRUCTIONS FOR COMPLETING THE BOWEL DIARY

In this folder you should find a copy of the Bristol Stool Scale and some of the diary pages that are colour-coded according to the stage in the trial in which you are using them – blue for pre-treatment, red for the first 4 weeks of electrical stimulation, yellow for the following 2 months.

1 The diary ***must be*** filled in each night before you go to bed, so you can remember what happened that day.

2 Make sure that ***each*** day has a date (day/month/year) and your code name is on it. This is the name you can choose so that your real name does not appear on any paperwork.

3 Under the column headed ***"Bowel action and type"***

- put a tick (√) for each bowel action you have.
- the tick goes in the 'sit' column if it happened as the result of going to the toilet to sit without any feeling of needing to poo.
- the tick goes in the 'spontaneous' column, if you went to the toilet because you had a feeling that you needed to poo.
- 'type' refers to the number that best describes the type of poo on the Bristol Stool Scale.

4 Under the column headed ***"Soiling"***

- put an 's' for each episode of soiling during the day.
- the 's' goes in the 'stain' column if the soiling was just a stain on the underwear.
- the 's' goes in the 'scrape' column if poo had to be scraped off before the underwear could be washed.

5 The column headed ***"Tablets, medicines, suppositories, enemas, washouts"*** is where you record the medicines etc.you had that day, and whether you had a bowel washout – just write "w.o." if you did.

6 The column headed ***"TENS today?"*** is to record the days that you have used TENS for your bowel.

7 The next column is to record whether you have ***"Tummy pain"*** or not on each particular day.

BOWEL DIARY SHEET	YOUR CODE NAME:

Date started / /	Bowel action and type		Soiling		Tablets Medicines Suppositories Enemas Washouts	TENS today? Yes/no ?Level	Tummy pain today? Yes/no	Comments
	Sit	Spontan-eous	Stain	Scrape				
MONDAY Date								
TUESDAY Date								
WEDNESDAY Date								
THURSDAY Date								
FRIDAY Date								
SATURDAY Date								
SUNDAY Date								

Remember √ = bowel action in toilet
S = episode of soiling
type = choose a number from the Bristol Stool Scale
w.o. = washout

APPENDIX H: Instructions for completing the Bowel Diary- EPM Trial

INSTRUCTIONS FOR COMPLETING THE BOWEL DIARY

In this folder you should find a copy of the Bristol Stool Scale and the diary pages

1 The diary ***must be*** filled in each night before you go to bed, so you can remember what happened that day.

2 Make sure that ***each*** day has a date (day/month/year) and your code name is on it. This is the name you can choose so that your real name does not appear on any paperwork. If you don't have a code name use your own name.

3 Under the column headed ***"Bowel action and type"***

- put a tick (√) for each bowel action you have.
- the tick goes in the 'sit' column if it happened as the result of going to the toilet to sit without any feeling of needing to poo.
- the tick goes in the 'spontaneous' column, if you went to the toilet because you had a feeling that you needed to poo.
- 'type' refers to the number that best describes the type of poo on the Bristol Stool Scale.

4 Under the column headed ***"Soiling"***

- put an 's' for each episode of soiling during the day.
- the 's' goes in the 'stain' column if the soiling was just a stain on the underwear.
- the 's' goes in the 'scrape' column if poo had to be scraped off before the underwear could be washed.

5 The column headed ***"Tablets, medicines, suppositories, enemas, washouts"*** is where you record the medicines etc.you had that day, and whether you had a bowel washout – just write "w.o." if you did.

6 The column headed ***EPM IF today?*** is to record the days that you have electrical stimulation for your bowel. Machine level means the number you reached on the scale on the left of the machine screen when you felt a comfortable tingling sensation.

7 The next column is to record whether you have ***"Tummy pain"*** or not on each particular day.

8 The last column is for any comments you want to tell us.

BOWEL DIARY SHEET	**YOUR CODE NAME:**

Date started / /	*Bowel action and type*		*Soiling*		*Tablets* Medicines Suppositories Enemas Washouts	*EPM IF today?* Yes/no Machine level	*Tummy pain today?* Yes/no	*Comments*
	Sit	Spontan -eous	Stain	Scrape				
MONDAY Date								
TUESDAY Date								
WEDNESDAY Date								
THURSDAY Date								
FRIDAY Date								
SATURDAY Date								
SUNDAY Date								

Remember √ = bowel action in toilet
S = episode of soiling
type = choose a number from the Bristol Stool Scale
w.o. = washout

APPENDIX I: Instructions - How to use your TENS Machine

HOW TO USE YOUR TENS MACHINE

The TENS you have been given consists of the machine itself, 2 sets of leads and 4 self-adhesive electrodes.

The settings on the machine have been set for your use and should not be altered. However the batteries will need to be replaced when it tells you on the screen by opening the battery compartment on the back of the machine.
Whilst the machine is being used it is possible to move around quietly, watch TV or read. But not to actively play or go outside. Be very careful the machine is not dropped. If it is necessary to stop treatment – to go to the toilet for example – press the on/off button and disconnect the leads from the machine. Leave the electrodes on the skin and resume treatment as soon as possible.

Care of electrodes
The electrodes need careful handling. They should be peeled off their backing or the skin by gently pulling on the corner of the electrode itself –NEVER by the lead. They should be applied to clean (washed with soap and water), dry skin –this is particularly important in warm weather.
After use they should be placed **immediately** back onto their plastic backing, press out all air bubbles between the electrode and backing, add 3 drips of water to the backing. **No** more. Store them flat in their sealed bag to prevent drying out and deterioration. If cared for in this way they should last for many uses.

When to throw out an electrode
DO NOT use an electrode if it does not stick all over to the skin.
When a corner starts to peel off it when you put it on the skin, throw it away and use a new electrode. If your child complains of a prickling sensation that wasn't there before, it may be because the electrode is not adhering well to the skin.
If skin becomes irritated or there are any problems with your machine, stop using it and contact your physiotherapist.

Janet Chase Ph: 9345 6458 or 9345 5805 (and leave a message)

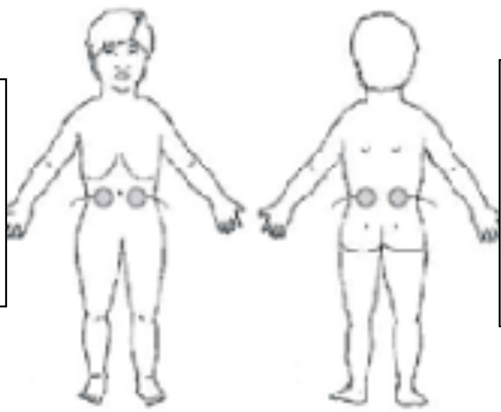
For further instructions please turn over the page………..

Machine settings & instructions:

There are 2 output sockets on top of the machine – the leads go into these.

- Remove covers from gel pad electrodes and place on skin as shown.
- Plug one lead into the output socket on the right and one in the left side of the unit.
- Connect the lead that comes from one socket to the electrode on the right side of the spine and its mate diagonally opposite on the left hand side of the tummy. Do the corresponding placement for the left lead.
- Open the cover and push the ON/OFF button
- Set the TIMER to 30 minutes
- DO NOT attempt to change MODE, P. WIDTH or FREQ –these are set.
- Press the CH1 and CH2 'up' arrows until a comfortable and equal sensation is felt under all 4 electrodes. If the sensation eases off after a few minutes then increase it again. If it is too strong press the 'down' arrows until comfortable.
- At end of session the machine will turn off, unplug leads and carefully remove electrodes from skin as previously described.
- Cover gel pads and store.
- Replace batteries when flashing battery symbol is shown on the display

The electrodes at the front are either side of the belly button below the level of the lowest ribs



The electrodes at the back are either side of the spine with 1-2 cm in between, at the level where the lowest rib joins the spine.

Remember to fill in your diary!

APPENDIX J: Instructions - How to use your EPM IF

HOW TO USE YOUR EPM IF

The EPM IF you have been given consists of the machine itself, the battery re-charger, 2 sets of leads (plus 1 spare lead) and 4 self-adhesive electrodes.

Prior to treatment charge the unit for 8 hours according to the instructions on page 3 of the manual, and return the unit to the charger in between uses.

This treatment is to be carried out 5-7 days per week for 30 minutes each time, and your diary is to be filled out daily.

Whilst the machine is being used it is possible to move around quietly, watch TV or read. But not to actively play or go outside. Be very careful the machine is not dropped. If it is necessary to stop treatment – to go to the toilet for example – press the on/off button and disconnect the leads from the machine. Leave the electrodes on the skin and resume treatment as soon as possible –you will need to reset the unit.

Care of electrodes
The electrodes need careful handling. They should be peeled off their backing or the skin by gently pulling on the corner of the electrode itself –NEVER by the lead or pigtail. They should be applied to clean (washed with soap and water), dry skin –this is particularly important in warm weather.
After use they should be placed **immediately** back onto their plastic backing, press out all air bubbles between the electrode and backing. Once per week add 2-3 drips of water to the back of each electrode. **No** more. Store them flat in their sealed bag to prevent drying out and deterioration. If cared for in this way they should last for many uses.

When to throw out an electrode
DO NOT use an electrode if it does not stick all over to the skin.
When a corner starts to peel off it when you put it on the skin, throw it away and use a new electrode. If your child complains of a prickling sensation that wasn't there before, it may be because the electrode is not adhering well to the skin.
If skin becomes irritated or there are any problems with your machine, stop using it and contact your physiotherapist.

Janet Chase Ph: 9345 6458 or 9345 5805 (and leave a message on the voicemail if necessary)

For further instructions please turn over the page……….

Machine settings & instructions:
There are 2 output sockets on the top of the machine marked Ch1 and Ch2.

- Remove covers from gel pad electrodes and place on skin as shown.

- Plug one lead into Ch 1 and one into Ch 2.

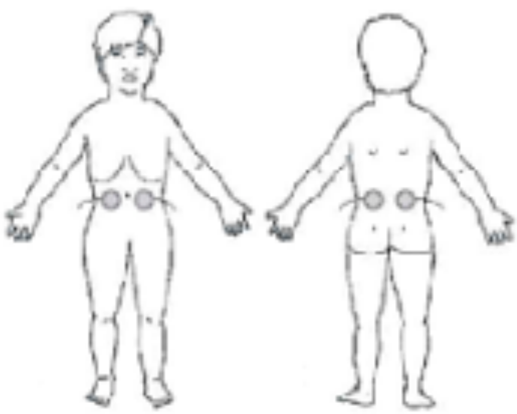
- Connect the lead that comes from the right socket to the electrode on the right side of the spine (red) and its mate diagonally opposite on the left hand side of the tummy (white). Do the corresponding placement for the left lead.

*The settings on the machine need to be set prior to **<u>EACH</u>** use as described below:*

- *Open the lid*
- *Press the on/off button once to turn machine on*
- *Press the **P button** (Program) until number 4 appears on the screen*
- *Press the **Freq control** (Frequency) until 80Hz reads on the screen*
- ***Pads** should be set for 4 pads (not 2)*
- *Press **Timer button** until 30 min appears on the screen*
- *Place the electrodes as described below*
- *Start the treatment by pushing the **Level button** repeatedly until a comfortable tingling is felt under all 4 electrodes. If this fades as treatment progresses –turn it up until the sensation is felt again. Make a note of this level on the scale on the left of the screen.*
- *The machine will turn off at the end of 30 minutes*
- *Disconnect leads from the electrodes, return electrodes to their plastic backing.*

WHERE TO POSITION YOUR ELECTRODES:

The electrodes at the front are either side of the belly button below the level of the lowest ribs



The electrodes at the back are either side of the spine with 1-2 cm in between, at the level where the lowest rib joins the spine.

Remember to fill in your diary!

APPENDIX K: Royal Children's Hospital Human Research Ethics Committee Approval (23040 C)

FILE COPY

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ISD (+613) 9345 5522
Facsimile (03) 9345 6769

ETHICS IN HUMAN RESEARCH COMMITTEE APPROVAL

EHRC REF. No:	**23040 C**
PROJECT TITLE:	Colonic manometry and transcutaneous stimulation (using interferential therapy) in Slow Transit Constipation.
Documents approved:	Module One dated July 2006, P/GIS and Consent v3 dated 11 July 2006. PIS and Consent v3 dated 11 July 2006. Previously approved: TGA No. L 27572 Bottom Line Newsletter V1, June 23 2003.
Approved Protocol:	Protocol within Module Two dated July 2006
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DATE OF APPROVAL EXPIRY: **15th May 2009**

SIGNED: 3/8/2006
COMMITTEE REPRESENTATIVE

APPROVED SUBJECT TO THE FOLLOWING CONDITIONS:

ALL PROJECTS

1. Any proposed change in protocol, or any approved documents, or the addition of any documents (including flyers, brochures, advertising material etc) and the reasons for that change or addition, together with an indication of ethical implications (if any), must be submitted to the Ethics in Human Research Committee for Approval prior to implementation.
2. The Principal Investigator must notify the Secretary of the Ethics in Human Research Committee of:
   - Any adverse effects of the study on participants and steps taken to deal with them.
   - Any unforeseen events.
   - Investigators withdrawing from or joining the project.
3. A progress report must be submitted annually and at the conclusion of the project, with special emphasis on ethical matters.
   Please note: It is the responsibility of the Investigator(s) to ensure that the RCH EHRC approval remains current for the entire duration of the project. Investigator's undertaking projects without current EHRC approval put at risk their indemnity, grant and publication rights.
4. All research information collected whilst individual participants are children, must be kept until the individual turns 25 (i.e 7 years after their 18th birthday).

DRUG TRIALS

5. The Investigator(s) must report to the Sponsor and the Ethics in Human Research Committee within 24 hours of becoming aware of any serious adverse event experienced by any subject during the trial.
6. The investigator(s) must ensure that all externally sponsored Clinical Drug Studies have insurance coverage that is current for the entirety of the study.

APPENDIX L: PinQ

1. I get shy because of my bladder problem

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

2. People in my family treat me in a different way because of my bladder problem

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

3. I am worried that people might think my clothes smell of wee

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

4. I think that my bladder problem won't get better

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

5. Mum and Dad worry about me because of my bladder problem

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

6. I would feel better about myself if I didn't have a bladder problem

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

7. My bladder problem makes me feel nervous

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

8. Mum or Dad sometimes seem a bit cranky because of my bladder problem

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

9. My bladder problem stops me going on sleep-overs or holidays

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

10. My bladder problem makes me feel bad about myself

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

11. I wake up during my sleep because of my bladder problem

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

12. I miss out on doing things because of my bladder problem

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

13. I feel unhappy because of my bladder problem

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

14. My bladder problem makes me feel sad

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

15. I think about my bladder problem when choosing what sport to play

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

16. I have to go to the toilet when I'm watching a movie

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

17. If my bladder problem was fixed I would invite more friends to my house

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

18. I choose hobbies that won't be spoilt by my bladder problem

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

19. My bladder problem makes me different to other people

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

20. I miss out on being with friends because of my bladder problem

☐ NO ☐ HARDLY EVER ☐ SOMETIMES ☐ OFTEN ☐ ALL OF THE TIME

NAME:______________________ DATE:_____________

APPENDIX M: List Of Abbreviations

BMI – body mass index

DES – dysfunctional elimination syndrome or combined bladder and bowel dysfunction

GIT – gastro-intestinal tract

GJH – generalised joint hypermobility

ICC – interstitial cells of Cajal

IFC – interferential current

PEDsQL – Pediatric Quality of Life Inventory

PEG – polyethylene glycol

PFM – pelvic floor muscles

QoL – quality of life

STC – Slow Transit Constipation

TENS – transcutaneous electrical nerve stimulation

APPENDIX N: Addendum

<u>Examiner 1</u>

Chapter 1.

Pages 28-30. Details of electrode placements in studies relating to electrical treatment of gastrointestinal tract motility have been inserted.

Page 37- repeat reference deleted

Chapter 2.

2.4.3 page 53. Inserted "Modification of their checklist, which may have altered its reliability and validity, resulted in a seven-question list, which was applied to the identified papers"

Chapter 3.

3.3.1 page 67. The following has been inserted –"These follow-up periods were based on the observation that children in the pilot study had long-lasting effects for at least two months after treatment."

3.3.2 page 68. The following has been inserted "any contraindication to the application of electrical current (diminished skin sensation, risk of skin irritation, cardiac pacemaker)"

3.3.5 page 69. Added "This treatment protocol was based on the recommendations of de Domenico (1987) who published the only previous work using IFC for STC."

Page 79, first paragraph as been changed to read "The intensity of stimulation was comfortable; so we *assumed* we did not stimulate A-δ or C-fibres"

Page 80. Final paragraph authors state "Transcutaneous electrical stimulation using IFC increased bowel motility, decreased bowel transit time, pain and soiling and improved physical quality of life in children with STC. More research is needed to determine optimum stimulation parameters including electrode position, parameters of current, *frequency* and duration of treatment."

Chapter 4.

Page 85. The text has been clarified thus –"After commencing the randomised controlled trial, a new portable battery-operated interferential machine became available *in Australia*"

Page 90. The following has been inserted into the text-"Two electrodes were placed either side of the spine in the curve of the back (T10-L2), each of these paired diagonally with two on the abdomen at the level of, and either side of the umbilicus"

Page 92 first paragraph. Both sets of figures have now been included. "In regard to spontaneous or sense–related bowel actions, the TENS group appeared to have a higher average number per week (3.48±2.12) compared to the IFC group (1.00±1.59)."

Chapter 5

Page 104. A preface has been added to explain the rationale for including a study on the musculo-skeletal characteristics of children with Slow Transit Constipation.

5.5.3.1 A reference has been added.

Figure 5.1a –lines have been superimposed to assist the reader.

5.5.8 These measures are known to be reliable but validity has not been established. See Chapter 6 page 139, final paragraph.

5.6.3 page 115, the following has been added to the text –"but it was not considered clinically significant because it may have been due to measurement error." The word "insignificant" has been removed from the text and replaced with "non-significant" as appropriate.

Figure 5.4 page 120. X axis has been clarified.

5.7.3 page 125, the following has been added to the text "However, we acknowledge that there might still be some difference in connective tissue behaviour, arrangement, extensibility or stiffness."

Chapter 6

6.3 page 136. Reference inserted

6.4.2 PinQ as reverenced in this section and included as Appendix K has been corrected.

Page 142. First paragraph inserted to discuss the weaknesses associated with incomplete data collection in Chapter 4.

6.6 The words "electrical stimulation" added to the concluding comments.

Examiner 2

Chapter 3. Abstract has been added, 3.1 page 65

3.3.9 page 70. The following has been added -"The geometric centres of radioactivity for the active and sham groups were compared before and after electrical stimulation by a *blinded* assessor."

3.3.10 page 70. The words "A daily bowel diary, completed through 16 weeks of the trial" have been added for clarity.

Table 3.1 Title has been corrected

6.4.2 page 142. Discussion added regarding the limitations of statistical analysis.

3.5 page 76. Sentence completed.

4.1 page 85. Words added to read as follows "They deliver up to 80mAmp current *intensity* with cycles up to 150Hz *frequency* and varying pulse width"

Figures 5.1a and 5.1b typographical errors corrected.

Examiner 3

TENS has been standardised through-out the text.

A list of abbreviations has been added as Appendix M, page 171.

3.2 Final sentence page 67. Typographical error corrected to read "quality of life".