Review Article

Pediatric gastrointestinal neuromodulation: A review

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Abstract

Neuromodulation, also known as bioelectric neuromodulation or neurostimulation, is the therapeutic use of electrical stimulation of nerves or brain centers. Neuromodulation has been trialed in an increasing range of human diseases as well as gastrointestinal disorders. The application of neuromodulation to treat pediatric motility and functional disorders is an exciting recent development. This review aims to briefly discuss the use of neuromodulation for the treatment of pediatric gastroparesis, constipation, and visceral hyperalgesia.

Keywords: Constipation, gastroparesis, neuromodulation, pediatric, visceral hyperalgesia

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INTRODUCTION

Neuromodulation, also known as bioelectric neuromodulation or neurostimulation, is the therapeutic use of electrical stimulation of nerves or brain centers. Neuromodulation has been trialed in an increasing range of human diseases including Parkinson's disease, arthritis, depression, pain and bladder dysfunction, as well as gastrointestinal disorders.[1] The application of neuromodulation to treat pediatric motility and functional disorders is an exciting recent development. This review article aims to briefly discuss the use of neuromodulation for the treatment of pediatric gastroparesis, constipation, and visceral hyperalgesia.

BACKGROUND

The background work regarding neuromodulation of the gastrointestinal tract goes back to over 100 years. Nobel Prize recipient (1906) Ivan Pavlov's work on digestive physiology and Nobel Prize recipients (1908) Camillo Golgi and Santiago Cajal's studies of nerve structure and function helped to lay the knowledge basis for future scientists to consider gastrointestinal neuromodulation.[2] The use of neuromodulation for the treatment of gastrointestinal disorders was reported as early as 1911 when electrical stimulation was delivered via saline enema to the colon for the treatment of constipation and ileus.[3] Further work in the 1920s led to the knowledge of gastrointestinal physiology, and in 1963, the concept of gastrointestinal pacing was proposed, along with a description of a gastrointestinal pacing device.[4,5] The use of neuromodulation for the treatment of gastrointestinal disorders has developed more rapidly over the past three decades and is now being used to treat symptoms including nausea, vomiting, constipation and fecal incontinence. Relatively, recently, these modalities have been applied to gastrointestinal disorders in children.[2,6]

Gastrointestinal sensory or motor dysfunctions (including disorders of gut–brain interaction, DGBI) can cause severe

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symptoms and negatively impact the quality of life for a significant number of patients. Some of these disorders include gastroparesis, postoperative ileus, constipation, fecal incontinence, and visceral hyperalgesia. In many patients, pharmacotherapy options to treat these disorders are limited and surgical intervention is usually thought of as the next available alternative. However, surgical resection of a dysfunctional gastrointestinal segment does not necessarily address the symptoms and may cause significant postoperative problems for the patient. Children with severe gastrointestinal symptoms that are refractory to medical treatment are especially faced with limited treatment options and neuromodulation can potentially serve as an intermediary treatment option prior to more invasive surgical procedures. The advantages of neuromodulation compared to medications and surgery are a minimal side effect profile, less invasive nature of the treatment, the ability to adjust treatment strength, and the inherent reversibility of the treatment; these are particularly valuable when treating pediatric patients.

The intrinsic innervation of the gastrointestinal tract (enteric nervous system [ENS]) has a complex two-way communication between the ENS and the central nervous system. The sensory-motor signals from the gastrointestinal system travel via the afferent limb of the vagus nerve and the spinal (thoracolumbar and sacral) nerves, to the brain where they are processed and perceived as symptoms. These central nerve connections provide opportunities for neuromodulation therapy.[1] Several different methods of gastrointestinal neuromodulation have been introduced.[2,7] Long-pulse stimulation was the earliest method used for pacing the gut and mainly activates muscles. Short-pulse stimulation is commonly used for nerve stimulation, and pulse train stimulation can activate both muscles and nerves.[8] In humans, neuromodulation has been applied at several sites on nerves innervating the gastrointestinal tract in experimental clinical settings to treat several gastrointestinal disorders, including vagal nerve stimulation for inflammatory bowel disease, vagal block for obesity, gastric electrical stimulation for nausea and gastroparesis, sacral nerve stimulation (SNS) and transcutaneous interferential electrical nerve stimulation for constipation/fecal incontinence, and percutaneous electrical nerve field stimulation (PENFS) for visceral hyperalgesia.[1] This review will focus on the use of gastric electrical stimulation, SNS, and percutaneous PENFS as therapies in pediatric patients with neurogastroenterologic disorders.

GASTRIC ELECTRICAL STIMULATION

Case: A 16-year-old female with Ehlers-Danlos syndrome (EDS) of the hypermobile type, and anxiety presented with chronic nausea for 3 years, worsening in frequency and severity with all meals; she also reported occasional vomiting, postprandial epigastric pain, and weight loss. Screening blood work, abdominal ultrasound, and upper endoscopy were normal. A 4-h, dual phase, gastric emptying scan was delayed for solids. Dietary modifications and pharmacotherapeutic trial with erythromycin, cyproheptadine, and prucalopride did not help. She underwent endoscopic pyloric Botox injection with balloon dilation three times and responded briefly only after the first two interventions. She eventually had an endoscopically placed temporary gastric electrical stimulator (GES) for 2 weeks and was able to eat 2 full meals a day with significant reduction of nausea and postprandial epigastric pain, resolution of vomiting, and had weight gain. Based on the success of the temporary gastric electric stimulation, a permanent GES was implanted subcutaneously with sustained improvement in her symptoms as well as psychological well-being.

Gastroparesis is a syndrome of objectively delayed gastric emptying in the absence of a mechanical obstruction and with certain cardinal symptoms including nausea, vomiting, early satiety, bloating, and abdominal pain. In children, most cases are idiopathic, with less common causes being drug-induced, postsurgical, or postviral.[9,10] Gastric electrical physiology and normal gastric motor functioning are complex and involve the sympathetic and parasympathetic nervous systems, the intrinsic ENS, and "pacemaker" interstitial cells of Cajal (ICCs). The proposed pathophysiology of gastroparesis includes decrease in ICCs and/or enteric neurons, autonomic denervation in viral gastroparesis, anatomical defects, medication related (such as narcotics), vagal nerve injury postgastric (including gastrostomy placement) or thoracic surgery, autonomic neuropathy, mitochondrial disorders, pyloric sphincter dysfunction, prematurity, constipation, and autoimmune gastrointestinal dysmotility.[11-19] Gastroparesis may be graded based on symptoms.[20] Patients with Grade 1 (mild) gastroparesis have intermittent, easily controlled symptoms with the maintenance of weight and nutritional status on dietary modification. Those with Grade 2 (compensated) gastroparesis have partially controlled symptoms needing medications including pain control, antiemetics, and prokinetics to control their symptoms and avoid hospitalizations. Patients with Grade 3 (gastric failure) gastroparesis do not respond to dietary modification or medication, cannot maintain nutrition or hydration orally, and end up needing frequent ER visits or admissions; for these patients, additional therapies including surgeries are considered. Supportive care including dietary interventions, enteral feeding via gastric or jejunal tubes, parenteral nutrition, and pharmacological and

endoscopic therapies for symptoms remain the mainstay treatment; however, the paucity of therapeutic trials in pediatrics limits the assessment of efficacy of medicines and there are no standardized guidelines for treating pediatric gastroparesis.[21,22] Concerns with the current therapies for gastroparesis include the potential for side effects when using medications, and the permanent changes and complications inherent in surgical options (including pyloroplasty, both surgical and endoscopic, and gastrectomy), and this underscores the need for novel therapies that are less invasive and potentially reversible that can be tried after failed medical and endoscopic treatments and prior to surgical intervention.

In 2000, the FDA approved the use of Enterra (Medtronic Inc., Minneapolis, MN) GES under the "humanitarian device exemption" for the treatment of diabetic and idiopathic gastroparesis for adults.[23] GES uses high-frequency, low-amplitude current delivered as a pulse, and the precise mechanism by which GES helps ameliorate symptoms of nausea and vomiting is not completely understood and appears to work through several mechanisms.[2] The early effects of GES include an improvement in nausea, vomiting, and feeding intolerance. Later, months after implantation of GES, effects on the hormonal and autonomic nervous systems have been described.[24] The rate of gastric emptying is not affected by GES and it has been proposed that it helps by improving gastric accommodation through stimulation of the ENS in addition to central (parasympathetic) effects mediated through the vagus nerve.[25]

Pediatric patients typically undergo a trial of temporary GES, where electrodes are endoscopically attached to the gastric mucosa of the greater curvature and antrum using endoclips and passed nasally or via a gastrostomy to be connected externally to a pulse generator [Figure 1]. They are followed clinically and with the help of questionnaires such as Patient Assessment of Gastrointestinal Disorders-Symptom Severity Index or Symptom Monitoring Worksheet for up to 2–4 weeks, to assess the symptom response. If the patient experiences greater than 50% improvement in their symptoms, they then undergo laparoscopic placement of a permanent GES, where electrodes are secured to the seromuscular layer of the greater curvature of the stomach connected to the pulse generator which is implanted in a subcutaneous pocket in the abdomen [Figures 2 and 3]. The patient is followed periodically and adjustments made to the pulse generator based on the symptoms. The GES has shown to be effective for reftractory nausea and vomiting associated with gastroparesis in both children and adults, with variable effects on gastric emptying.

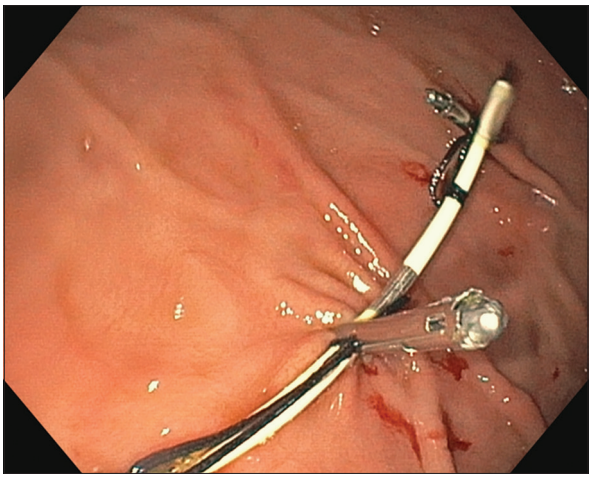

Figure 1: Temporary GES leads placed during an upper endoscopy (leads clipped to the gastric mucosa)

Several studies have been published showing that GES in adult patients is effective and safe and can improve the severity of symptoms in adults. An adult study showed that GES improved gastroparetic symptoms in patients with medically refractory nausea and vomiting at 6 months and sustained at 12 months.[26] However, in pediatrics, there is limited data with only a few published studies so far. The largest pediatric study enrolled 97 children over a period of 10 years.[27]

GES is being increasingly used in pediatric patients, as young as 2 years of age, and has been shown to be safe and effective with symptom improvement over 1 year with pediatric patients with gastroparesis.[27] GES has also been shown to significantly improve symptoms (nausea, fullness, early satiety, bloating, epigastric pain, vomiting) as well as quality of life for patients with functional dyspepsia.[28,29] There is a significant decrease in medication use after GES, most notably with antiemetics and prokinetics but not with pain medications or antireflux medications, and a decreased need to maintain a restricted diet.[27] Furthermore, studies in pediatrics have shown a significant improvement in the quality of life, reduction in the total number of hospitalizations, and reduced costs for both patient and the healthcare network.[27-29] A recent prospective study looking at long-term outcomes showed 90% improvement in symptoms leading to permanent GES placement as well as a significant decrease in the use of tube feeds or parenteral nutrition. This study also showed that factors predictive of a positive short-term GES response in children included more severe baseline vomiting and nausea but not age, gender, or pain level; the probability of a long-term response was independent of the initial symptoms. Furthermore, a diagnosis of delayed gastric emptying was not found to be associated with a positive response to GES.[30]

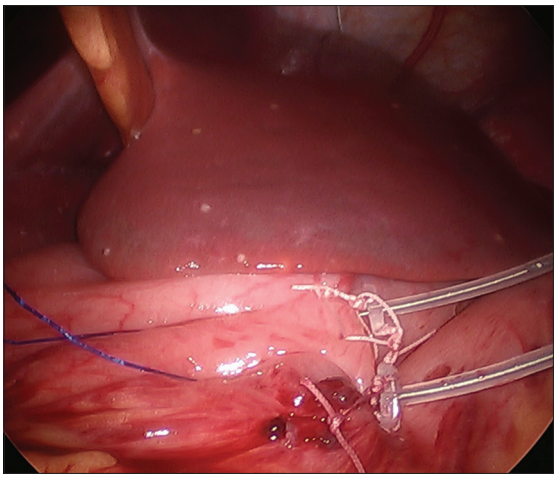

Figure 2: Permanent GES leads placed during laparoscopy (leads sutured to the outside of the stomach)

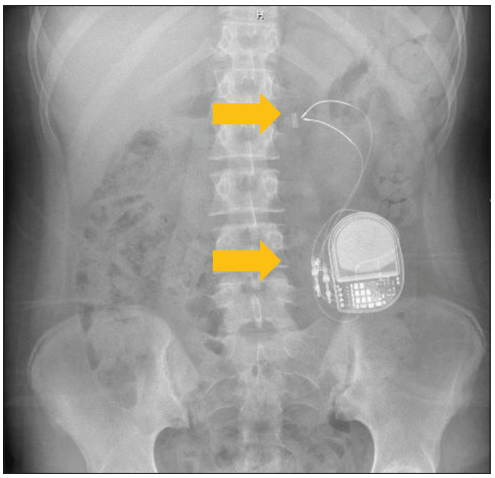

Figure 3: Permanent GES as seen on an abdominal X-ray (yellow arrows showing the leads in the upper left and pulse generator in the lower left of the patient)

The complication rate of 16–20% includes abdominal pain, battery replacement, replacement of electrodes, and infection. Overall, GES is considered feasible, well-tolerated, and safe (short and long term) in children.[27,29]

SACRAL NERVE STIMULATION

Case: A 13-year-old female patient, with no comorbid conditions, presented with constipation of 1 year without soiling. Multiple medications and dietary modifications were tried without significant improvement. She was having bowel movements 1–2 times per week with hard rock-shaped or watery stools (Bristol stool chart 1 or 7, respectively) despite taking daily stimulant laxatives and needing bowel clean outs weekly. She was home-schooled due to the severity of her constipation affecting her quality of life and well-being. Her work up included screening blood tests, water-soluble contrast enema, and MRI spine which were all reported normal. Upper and lower endoscopy with colonic manometry as well as anorectal manometry were performed and were normal. Despite escalation of her laxative doses (up to Senna 100 mg and milk of magnesia 933 mg once daily, Linaclotide 145 mg twice daily, and with weekly bowel clean outs), her symptoms persisted. She underwent Stage 1 (temporary/external) placement of sacral nerve stimulator (SNS) and reported significant improvement in the frequency of spontaneous bowel movements so as to be able to wean off some of her laxatives. Two weeks later, after showing adequate response, she underwent Stage 2 (permanent) placement of SNS and was able to decrease daily laxative doses and discontinue the weekly clean outs and is able to return to school.

Functional constipation is a common problem in children and is characterized by infrequent, hard painful stools with or without abdominal pain or fecal incontinence.[31] Constipation causes significant distress to the child and family and significantly impacts health care cost.[32] The nerve pathways for voluntary control of defecation and fecal incontinence are complex and involve neurons that project to the spinal defecation center in the intermediolateral column at the sacral S1 level, and this center connects with intrinsic reflex pathways of the ENS via the pelvic ganglia. The precise mechanism of SNS is unclear, but it is thought that SNS modulates an orectal function at the pelvic afferent or central level.[33]

Although most children respond to conventional medical and behavioral treatment, many continue to have symptoms.[34] Treatment options for children with medically refractory constipation are limited and more invasive therapies such as anal sphincter Botox injection and dilation, transanal enemas, antegrade continence enemas, colonic diversion, and partial or total colonic resection may need to be considered.[34,35] Just like the GES for gastroparesis and functional dyspepsia, SNS can be considered a bridge therapy before considering more invasive surgical therapies. SNS offers direct sacral nerve low-amplitude electrical stimulation of the sacral nerves via an electrode placed through the sacral foramen that is connected to a pulse generator implanted with the gluteal subcutaneous fat. SNS was FDA approved in 1997 for adults with urinary incontinence and then in 2012 for adults with fecal incontinence or constipation and since then has been established as a first line therapy for adults with treatment refractory fecal incontinence.[36-38] Like the GES, the placement of SNS involves a two-stage procedure. The first stage procedure involves placement of a lead at the S3 sacral nerve root; the lead is then connected to

a temporary pulse generator that remains external to the patient [Figure 4]. The patient's symptoms are monitored for a 2-week period, and if improved (greater than 50% improvement in baseline symptoms), they then undergo the second stage procedure, which involves implantation of a permanent pulse generator into the subcutaneous tissue of the glute [Figure 5]. The InterStim® System (Medtronic, Inc., Minneapolis, MN, USA) is the SNS that has been used most commonly.

Over the past two decades, experience with the use of SNS to treat adults with constipation and fecal incontinence has increased and is now being increasingly used in pediatric patients.[38-43] While adult studies showed no significant improvement for constipation alone, the benefit of SNS in children with constipation was noted after studies initially showed improvement in constipation and fecal soiling of children who received the SNS for their dysfunctional elimination syndrome.[39,44-46] Studies that followed showed symptomatic improvement (increased defecation frequency, decreased abdominal pain) in pediatric patients with functional constipation and improved quality of life for pediatric patients with constipation (functional and imperforate anus) refractory to conventional therapy.[41,42] A recent prospective study looked at pediatric patients who had been treated with antegrade cecostomy enemas (ACE) for constipation with and without fecal incontinence refractory to conventional therapy and underwent SNS placement, following them for more than 2 years; the majority of these patients had functional constipation, while some had anorectal malformation, tethered spinal cord, and Hirschsprung's disease. Overall, there was no change in defecation frequency (the majority of research subjects had more than three bowel movements weekly) over the study period; however, there was a statistically significant improvement in fecal and urinary incontinence, and there was a decrease in abdominal pain. Patients with functional constipation did have statistically significant improvement in fecal and urinary incontinence as well as abdominal pain. Patient-reported outcomes were significantly improved over the study period, including the Gastrointestinal Symptom Scale, Fecal Incontinence Quality of Life Scales, and Fecal Incontinence Severity Index. Furthermore, that study showed that overall the number of patients using oral laxatives decreased with the SNS placement and the number of patients using ACE had significantly decreased (decreased in functional constipation) and that SNS can be beneficial for children with constipation regardless of the presence of fecal incontinence.[47] A retrospective review of pediatric patients with functional constipation and functional incontinence who were treated with either ACE or SNS showed that although both ACE and SNS lead to improvement in both pediatric functional constipation and functional incontinence, SNS was more effective for functional incontinence and ACE was more effective for improving bowel movement frequency, abdominal pain, and laxative discontinuation.[48]

A review of adverse events of SNS in 1954 patients with fecal incontinence pooled from different reports showed an overall reoperation rate of 18.6% to explant or replace the device or lead or to revise the generator pocket.[49] Almost a quarter of pediatric patients with refractory constipation had complications from SNS requiring further surgery, including a local infection of the subcutaneous pocket, or a displacement or malfunction of the SNS. Regardless, most patients reported that they would proceed with the SNS if they were given the opportunity to remake their decision.[47]

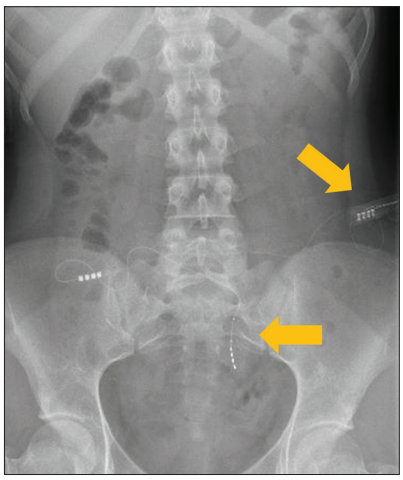

Figure 4: Temporary SNS leads as seen on an abdominal X-ray (yellow arrows showing the lead on the lower left and external pulse generator on the upper left of the patient)

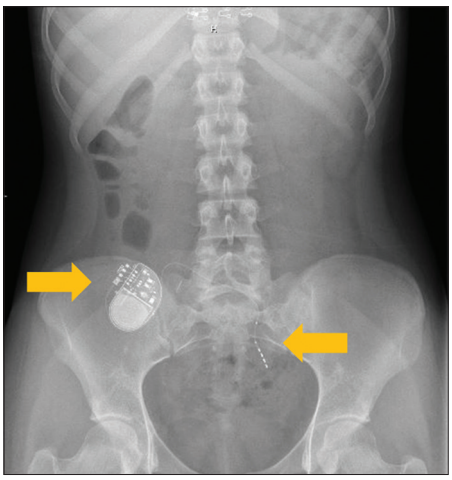

Figure 5: Permanent SNS as seen on an abdominal X-ray (yellow arrows showing pulse generator on the right and lead on the left of the patient)

Recently, the results of a pilot study of noninvasive SNS to treat pediatric constipation were presented. Pediatric patients with chronic constipation were treated with a stimulation device attached to adhesive electrodes placed on the lower abdomen and back and generated an electrical field (frequency of 15 Hz via stimulation intensity of 1–10 V); more than half of the patients demonstrated an improvement in their constipation, with sustained improvement in half of those patients. Minor complications such as skin irritation and electrode displacement were noted.[50]

A recent systematic review and meta-analysis of adult trials of lower gastrointestinal electrical nerve stimulation for fecal incontinence and constipation showed that sham stimulation is associated with clinical and statistically meaningful improvements in symptoms and quality of life scores of these patients. This highlights the importance of sham controls in nerve stimulation trials and the significance of placebo effect with neuromodulation.[51]

PERCUTANEOUS ELECTRICAL NERVE FIELD STIMULATION

Case: A 17-year-old female patient presented with chronic nausea (without vomiting), abdominal pain, and constipation, without weight loss, of 11 months duration. She reported improvement of her constipation on laxatives but no improvement of her nausea. She also reported anxiety which worsens her nausea. A trial of cyproheptadine as well as pyloric Botox injection and balloon dilation were not helpful. She saw a counsellor and had a trial of antianxiety medication, both of which did not help. Due to the severity and chronicity of her nausea and abdominal pain, she had significant school absenteeism and was concerned about her ability to graduate. Work up, including screening blood tests, MRI brain, upper endoscopy, and antroduodenal manometry, were normal, and she was diagnosed as having a DGBI and visceral hyperalgesia. She underwent PENFS with an auricular device (IB-Stim) with which her nausea and abdominal pain improved significantly; she also reported being more energetic, able to engage more socially, and able to complete her requirements for graduation.

DGBI, previously referred to as functional gastrointestinal disorders (FGIDs), include disorders characterized by gastrointestinal symptoms in the absence of other causative conditions. DGBI include irritable bowel syndrome (IBS), functional dyspepsia, and functional abdominal pain. They account for about 50% of pediatric gastroenterology visits in the USA and are the most common chronic pain conditions of childhood, associated with significant functional disability, impaired quality of life, and a large health care cost burden.[52-54] The management of DGBI is challenging, given the complex multidimensional nature and poorly understood pathophysiology. Pharmacologic treatments have been largely suboptimal, and a systemic review found no evidence to support the use of pharmacological agents in DGBI due to lack of high-quality trials.[55,56] PENFS is a novel, noninvasive approach to treat patients with functional nausea, functional abdominal pain, and other DGBI.

Modulating central pain pathways via electrical stimulation of the brain is a potential therapeutic mode for addressing pain in DGBI. The desire to access these central pathways with a peripheral or noninvasive method led to the development of PENFS delivered via an auricular device that provides alternating frequencies of stimulation to target central pathways through branches of cranial nerves V, VII, IX, and X that innervate the external ear.[57] A study on a rat model of postinflammatory hyperalgesia showed that PENFS decreases amygdala and lumbosacral spinal neuron firing and modulates visceral hypersensitivity.[58]

A randomized, sham-controlled trial on adolescents aged 11–18 years who met Rome 3 criteria for abdominal pain-related FGIDs showed that PENFS was overall beneficial and provided sustained efficacy. Patients with the device, compared to patients with a sham device, had a statistically significant greater reduction in worst pain after 3 weeks, and this difference was sustained for an extended period (median follow up of over 9 weeks).[59] It also showed statistically significant improvement in the functional disability inventory scores in those patients with the device as compared to those with the sham device.[59] Furthermore, auricular neurostimulation has been shown to reduce abdominal pain scores and improve the overall wellbeing in adolescents with IBS.[60] Impaired cardiac vagal regulation measured by vagal efficiency has been shown to predict pain improvement with auricular neurostimulation.[61]

In our recent study in 20 adolescents aged 11–19 years with functional abdominal pain disorders (FAPD), we analyzed the effects of PENFS on gastric mechanosensitvity through a water load symptom provocation task (WL-SPT), sleep and psychological functioning, as well as long-term outcomes.[62] Evoked pain intensity and nausea during WL-SPT were lower following PENFS compared to baseline ($P = 0.004$ and $P = 0.02$ respectively). Self-reported sleep quality, insomnia severity, sleep disturbance, and sleep-related impairment improved after

PENFS (*P*'s < 0.05) as well as actigraghy-derived sleep onset latency ($P = 0.03$). There were improvements in Abdominal Pain Index ($P < 0.0001$), pain catastrophizing ($P = 0.0004$), somatic complaints (0.01), functional disability ($P = 0.04$), and anxiety ($P = 0.02$) after PENFS, with some effects sustained at 6–12 months post-treatment. Thus, PENFS appears to be a suitable treatment for FAPD affecting multiple factors associated with GI symptoms.

In another yet unpublished retrospective study in patients with FAPD, we have assessed the outcomes of PENFS with behavioral interventions compared to PENFS alone ($n = 115$).[63] Improvement in subjective physician response to abdominal pain ($P = 0.02$) and nausea ($P = 0.04$) and a trend toward improvement of constipation and sleep were noted with each subsequent visit and follow-up visits up to 12 months. The total scores for abdominal pain index ($P < 0.001$), nausea severity scale ($P < 0.001$), anxiety ($P = 0.001$), depression ($P = 0.003$), sleep quality ($P = 0.001$), somatic complaints ($P < 0.001$), and functioning ($P < 0.001$) improved with each subsequent visit and follow-up. The combined group had greater improvement in symptom response for constipation at 3 weeks ($P = 0.05$) and improvement in sleep at 3 months post-treatment follow-up visit ($P = 0.04$) compared to PENFS alone. Other subjective symptom responses and the total scores were lower in the combined group at 3 weeks and 3 months post-treatment follow-up compared to PENFS alone, but were not statistically significant.

The FDA recently approved PENFS for adolescents 11–18 years of age with functional abdominal pain associated with IBS. The device is placed in a clinic by a certified physician. The ear is transilluminated to mark the neurovascular branches so that the leads are placed at the appropriate location on the dorsal and ventral aspects of the ear within 1 mm of the vascular branches at four sites [Figure 6]. The patient wears the device five consecutive days each week and removes it at home, returning to clinic after the device has been off for 2 days, each week for four consecutive weeks.

No serious adverse events were reported in the sham-controlled study. Some side effects noted included mild ear discomfort, mild dermatitis from adhesive allergy, syncope due to needle phobia, bleeding; there were no infections.[59,64] This therapy is contraindicated in patients with titanium allergy, cardiac pacemakers, hemophilia, psoriasis vulgaris and in pregnant patients. Data is not available for use in patients with seizures, severe cardiac disorders, or concurrent gastric, or vagal or SNSs (can consider use if devices can be turned off). The therapy may be challenging for patients with autism spectrum disorder, developmental delays, and procedural anxiety.

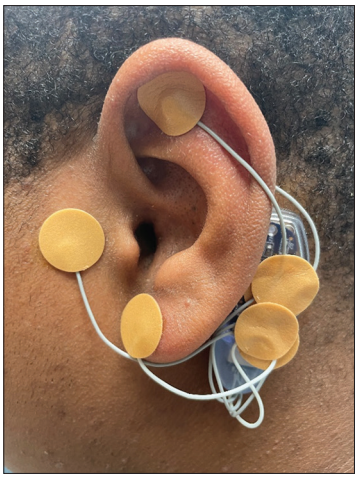

Figure 6: Percutaneous electric nerve field stimulation applied to the ear (patient consent obtained)

Future studies may shed light on the applicability and efficacy of PENFS in other DGBI as PENFS is also being used in other FAPDs like functional dyspepsia, abdominal migraine, and functional abdominal pain, not otherwise specified (FAP-NOS).

FUTURE PROSPECTS

The use of neuromodulation to treat sensory and motor gastrointestinal conditions continues to evolve, and we can expect new therapies to emerge. Some of these are briefly described below.

Abdominal transcutaneous electrical stimulation (TES) delivers an interferential current through four abdominal surface electrodes; an interferential current is a type of current to overcome skin impedance to allow optimal benefit of that current to the target site, or nerve, of interest.[65] Abdominal TES has been shown to improve chronic constipation in pediatric patients who did not improve with conventional therapy.[66] A home-based abdominal TES therapy was shown to be feasible, and children with slow transit constipation treated with the home-based therapy had clinically significant improvement in defecation frequency, soiling, abdominal pain, urge to defecate, and quality of life.[67-69]

Posterior tibial nerve stimulation (PTNS) involves electrical stimulation of the posterior tibial nerve at the level of the ankle, either percutaneously with a needle or transcutaneously with an electrode. This stimulation of the tibial nerve is thought to stimulate the sacral

nerves leading to modulation of urinary and defecatory function, somewhat like SNS. The use of PTNS to treat adult refractory constipation has been shown to be well tolerated and affordable.[70,71] Experience with PTNS in children is currently primarily limited to treatment of urinary dysfunction.[72] A study of home-based transcutaneous PTNS for pediatric fecal incontinence showed improvement and or resolution; however, there was a recurrence with discontinuation.[73] More studies are investigating further the use of PTNS for treating pediatric functional constipation.[74]

Translumbosacral neuromodulation therapy involves painless magnetic stimulation of nerves that regulate muscles in the anus and rectum. An adult study showed significant improvement in fecal incontinence in the short term as well as improved anorectal neuropathy and physiology and is being seen as a novel and safe, efficacious, and noninvasive treatment for fecal incontinence.[75]

Sensory and motor dysfunctions of the gastrointestinal tract can cause severe symptoms and significantly decrease quality of life. Neuromodulation of the gastrointestinal tract is a new and valuable addition that enriches the armamentarium of treatment options. Some of the challenges with neuromodulation include understanding the precise mechanisms of its actions, identifying the right patient, achieving a beneficial and clinically significant therapeutic end point, achieving disease modification in addition to symptomatic improvement, safety, optimizing modulation parameters and location, monitoring effectiveness of modulation, and maintaining its effectiveness long term. Even though results have been promising thus far, further research is needed before there is more widespread acceptance of neurostimulation in the treatment of children with sensory-motor disorders of the gastrointestinal tract.

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Conflicts of interest

There are no conflicts of interest.

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