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REVIEW ARTICLE

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Transcutaneous electrical stimulation for gastrointestinal motility disorders

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Abstract

Background/Purpose: Gastrointestinal (GI) dysmotility is categorized by muscle or nerve dysfunctions in any portion of the GI tract, which leads to abnormalities in GI motor and sensory function. Symptoms may vary depending on the organ affected and can be debilitating. Treatment usually involves diet and lifestyle changes. Pharmacotherapy is limited in effectiveness with various side effects. Transcutaneous electrical stimulation (TES), a noninvasive, needleless technique that provides electrical stimulation using cutaneous non-needle electrodes, has become increasingly popular. It has been shown to be beneficial in treating GI motility disorders.

Methods: This review paper navigates through the different TES techniques, including transcutaneous peripheral nerve (vagal/sacral/tibial nerves) electrical stimulation, transcutaneous electrical acustimulation (stimulation via acupuncture point), transcutaneous interferential current therapy, and transcutaneous electrical nerve stimulation.

Key Results: As we delve deeper, we explore the promising effects of TES on dysphagia, gastroesophageal reflux disease, functional dyspepsia, gastroparesis, postoperative ileus, constipation, and irritable bowel syndrome. The literature at hand speaks volumes about the therapeutic prowess of this noninvasive technique.

Conclusion & Inferences: The time is ripe to evaluate further the full therapeutic potential of TES, a noninvasive, nonpharmaceutical, nonsurgical, and home-based self-administrative technique in managing GI motility disorders.

KEYWORDS

acustimulation, gastrointestinal motility, transcutaneous electrical stimulation, transcutaneous interferential current, vagus nerve stimulation

1 | INTRODUCTION

Gastrointestinal (GI) motility disorders can occur when the nerve or muscles in the GI tract do not work in a coordinated way.[1] Symptoms may vary depending on the organ affected and can significantly impact the quality of life. GI motility disorders include dysphagia, gastroesophageal reflux disease (GERD), gastroparesis, functional dyspepsia (FD), chronic intestinal pseudo-obstruction (CIPO), constipation, and irritable bowel syndrome (IBS), among others.[2] Therapy is mainly focused on diet and lifestyle modification, and pharmacotherapies are limited in effectiveness with various side effects.[2]

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Transcutaneous electrical stimulation (TES) provides electrical stimulation using surface electrodes. It has become increasingly popular because it is a noninvasive, needleless, and self-administrative technique that is well tolerated by patients. It has been shown to be beneficial in treating GI motility disorders.[3–5]

This review paper will discuss the different TES techniques available, including transcutaneous peripheral nerve stimulation (TPNS), transcutaneous electrical acustimulation (TEA), transcutaneous interferential current (IFC), and transcutaneous electrical nerve stimulation (TENS). Additionally, this paper will review the available TES studies in GI motility disorders of the esophagus, stomach, small intestines, and colon.

Key points

- GI motility disorders have a significant impact on patients' quality of life, and current treatment options have limitations. However, promising results have been observed with the use of noninvasive transcutaneous electrical stimulation (TES) techniques.
- TES techniques, including transcutaneous peripheral nerve stimulation (TPNS), transcutaneous electrical acustimulation (TEA), transcutaneous interferential current (IFC), and transcutaneous electrical nerve stimulation (TENS), show efficacy in improving symptoms and functions associated with esophagus, stomach, small and large intestines.
- By modulating the autonomic nervous system, TES techniques target specific nerves and acupuncture points to influence GI motility, sensation, and secretion. This novel approach holds promise for effectively managing GI motility disorders and improving patient outcomes.

2 | METHODOLOGY OF TRANSCUTANEOUS ELECTRICAL STIMULATION

Transcutaneous electrical stimulation is a promising therapeutic option for GI motility disorders. TES is usually delivered in less than 60 min each time and from once every other day to twice daily. The different TES techniques include, TPNS, TEA, IFC, and TENS which are described below.

2.1 | Transcutaneous peripheral nerve stimulation

Transcutaneous peripheral nerve stimulation is a noninvasive technique that involves the delivery of electrical currents on the skin to stimulate specific nerves.[6] The electrodes are placed at or near the nerves of the designated treated area.[6] It is commonly used to treat chronic pain but has shown favorable results in treating GI disorders.[7–12] The main techniques include transcutaneous vagal nerve stimulation (tVNS), transcutaneous sacral nerve stimulation (tSNS), and transcutaneous tibial nerve stimulation (tTNS) (Figure 1A–D).

tVNS has become of particular interest because it is noninvasive with better safety than VNS using implantable electrodes, which may cause infection, bleeding, bradyarrhythmias, and respiratory dysfunction.[13] tVNS uses a battery-powered neurostimulator and stimulates the myelinated sensory afferent vagus nerve fibers within the carotid sheath inside the neck.[8,13] Studies have proved that tVNS has similar efficacy as VNS using implantable electrodes via functional MRI and peripheral sympathetic tone measurements.[14,15] Two main techniques of tVNS include transcutaneous auricular vagal nerve stimulation (taVNS, see Figure 1A) and transcutaneous cervical vagal nerve stimulation (tcVNS, see Figure 1B). tcVNS is performed non-invasively using a portable powered stimulator that has steel contact electrodes. Subsequently, the stimulator is applied to the neck to deliver electrical stimulation to the vagal nerve.[8,13] In taVNS, small surface electrodes are placed near the concha in the ear to elicit a diffuse stimulation field, which activates the auricular branch of the vagus nerve.[16,17] This activation is known to trigger the same brain areas as invasive VNS.[18] The therapeutic stimulation frequency is usually between 0.5 and 30 Hz. Relatively higher stimulation frequencies of 20–30 Hz are used to increase vagal nerve activity, while lower frequencies of 0.5–10 Hz are required to manipulate sympathetic nerve activity.[13,19]

Both tSNS (Figure 1C) and tTNS (Figure 1D) have been used for GI motility of the lower tract.[20] tSNS uses low-level electrical stimulation over the nerves of the sacral plexus. The sacral plexus innervates the perineum, and tSNS has been shown to be beneficial in treating lower bowel dysfunction and muscle function of the anal canal.[21,22] The tSNS stimulation frequency is usually between 10 and 50 Hz.[23,24] tTNS is delivered using a surface electrode over the tibial nerve's most superficial position, which is superior and posterior to the medial malleolus.[11,25] It is believed that stimulation of the tibial nerve modulates defecatory function by activating sacral nerves.[11,20,26] The stimulation frequency used for tTNS is between 10 and 25 Hz.[27,28]

2.2 | Transcutaneous electrical acustimulation

Transcutaneous electrical acustimulation (Figure 1E; previously called transcutaneous electroacupuncture) is a noninvasive, needless technique that delivers electrical stimulation on the skin at the acupuncture point sites via surface electrodes. This method evolved from traditional Chinese acupuncture or electroacupuncture, which involved a needle puncturing into an acupuncture point.[29] It has been used to treat GI disorders.[29–32] The most commonly used acupuncture points are Neiguan (PC6) and Zusanli (ST36) when treating GI disorders.[31] In prior studies, TEA was delivered as an easily wearable watch-like device.[33–35] It typically uses intermittent stimulation parameters, including a frequency of 5–100 Hz, pulse width equal

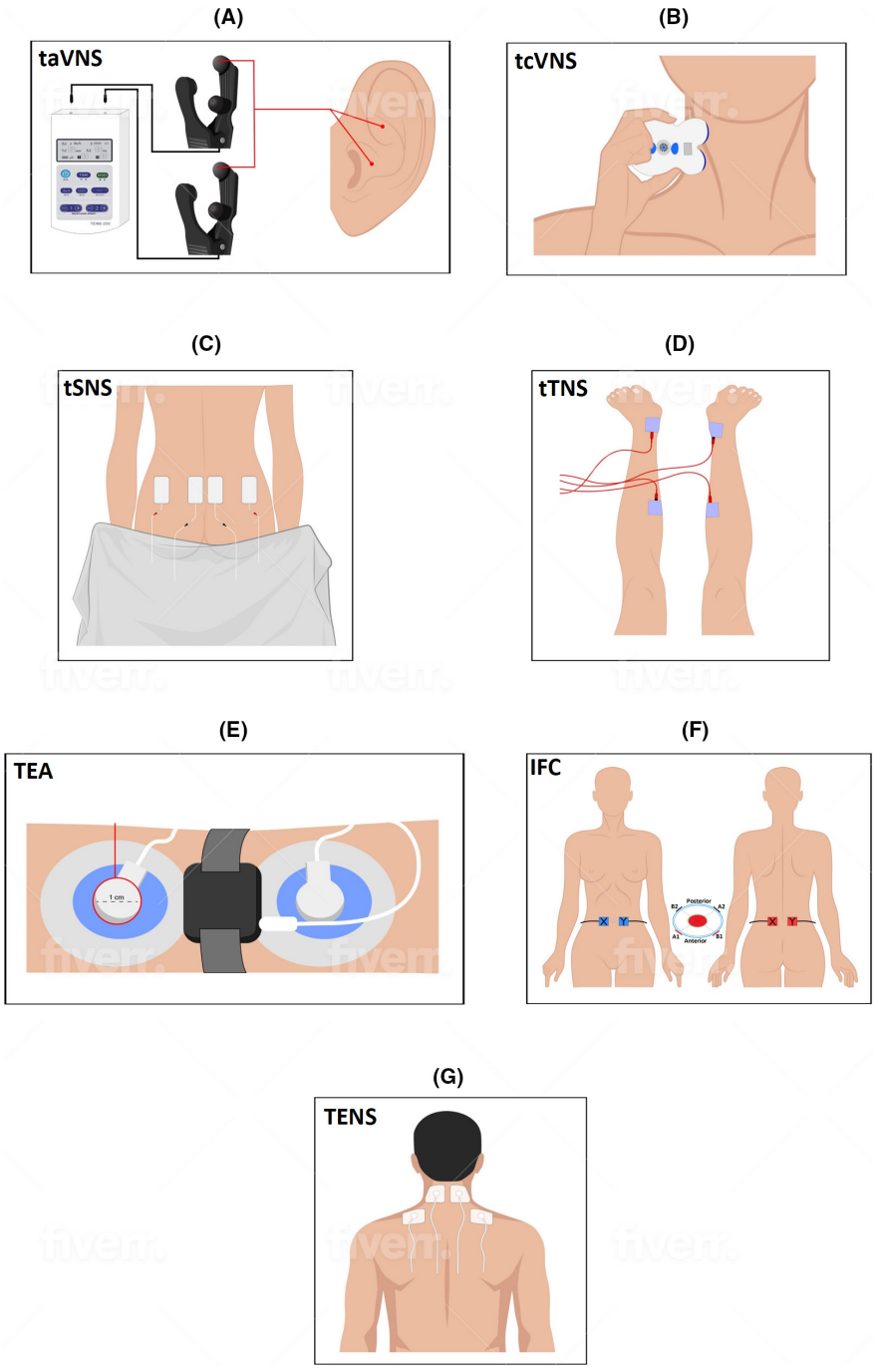


FIGURE 1 Transcutaneous electrical stimulation (TES). (A) Transcutaneous auricular vagal nerve stimulation (taVNS); (B) transcutaneous cevical vagal nerve stimulation (tcVNS); (C) transcutaneous sacral nerve stimulation (tSNS); (D) transcutaneous tibial nerve stimulation (tTNS); (E) transcutaneous electrical acustimulation (TEA); (F) transcutaneous interferential current (IFC); (G) transcutaneous electrical nerve stimulation (TENS).

to or greater than 0.3 ms, and amplitude of 1–10 mA, depending on patient tolerability.[32,33,36,37]

2.3 | Transcutaneous interferential current

Interferential current (Figure 1F; interferential therapy or interferential current transcutaneous electrical sensory stimulation) dates back to the 1950s. IFC was initially used to treat genitourinary dysfunctions.[38–40] Subsequent studies found promising results in treating GI motility. The current is produced at the bisection of two diagonally opposed currents by their interference with one another.[38] It generates a medium frequency current by using two sinusoidal waves that are crossed and interfered with each other, creating a third vector that penetrates nerve fibers deep in target organs.[38,39,41] A 4–10 kHz carrier frequency for two currents has been used in IFC.[42] However, 4 kHz was found to have better tolerability and is optimum at penetrating deeper tissue.[42]

2.4 | Transcutaneous electrical nerve stimulation

Transcutaneous electrical nerve stimulation (Figure 1G) is a non-invasive peripheral stimulation technique commonly used to treat

chronic pain. TENS is usually applied to nerve dermatomes or areas of muscle pain.[36] Similarly to TEA, TENS may also be applied to acupoints. However, TENS stimulates a larger area than TEA, and the pulse width is commonly less than 0.3 ms.[36] It has become of particular interest in treating functional GI disorders and has been shown to improve GI motility.[43] Electrodes are placed in the affected area, and the purpose is to activate large-diameter non-noxious afferents to reduce nociceptive cell activity and sensitization.[44]

3 | MECHANISMS OF ACTION

The autonomic nervous system (ANS) is composed of the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS). The SNS and PNS are two interconnected branches of the autonomic nervous system, which have distinct yet complementary roles in regulating physiological functions. While it has been previously proposed that an imbalance between them may contribute to GI dysmotility, current knowledge suggests that their relationship is more complex and involves dynamic interactions, rather than a simple balanced model.[45] It is believed that TES such as tVNS, TEA, and TENS works by modulating the ANS.[13,16,46,47] The vagus nerve and sacral plexus are part of the PNS and play an important role in regulating interactions between the central nervous system and the GI tract, including functions of the esophagus, stomach, small bowel, and colon. It regulates motility, sensation, and secretion and maintains the intestinal barrier.[27,48] The vagus nerve is composed of 80% afferent fibers and 20% efferent fibers, with PNS neurons transmitting afferent information from the GI tract to the brainstem, conveying efferent information from the brainstem to the GI system to perform its actions on the GI tract, such as motility and sensation. In clinical trials, vagal activity is frequently evaluated using heart rate variability (HRV). HRV is a noninvasive measurement derived from electrocardiograms and spectral analysis of R-R intervals. It has been extensively employed for assessing vagal activity in various GI motility disorders, as detailed in Tables 1–3.

Although the precise mechanism of IFC remains to be fully elucidated, current research suggests that it may involve multiple processes. One potential mechanism is neuromodulation and alternation in neuroplasticity of the enteric nerves, which could lead to structural or synaptic changes.[42] These changes may subsequently result in modified neuronal function and improved GI motility.[38,42] Additionally, IFC is hypothesized to exert its effects by stimulating the interstitial cells of Cajal (the pacemakers cells of the gut) which are responsible for generating and propagating electrical slow waves that coordinate gut contractions.[38,42] Furthermore, IFC may also influence the enteric autonomic nervous system, which plays a vital role in regulating GI function and motility. By targeting these different components, IFC could potentially enhance overall GI function and provide therapeutic benefits for patients with GI motility disorders.[38,42]

Vasodilators have been used to treat GI disorders by enhancing smooth muscle relaxation.[2] It is hypothesized that TENS may cause an increase in blood flow and allows for the release of neuropeptides.[49] Zhang et al.[49] found that TENS increases local blood flow in the treated area in their animal study, which likely contributes to its mechanism of action. TENS studies have found increased activity by neurochemicals, including acetylcholine, noradrenaline, gamma-aminobutyric acid, serotonin, nitric oxide, and opioid receptors.[35,50] Additionally, studies suggest a decrease in the activity of plasma vasoactive inhibitory peptide and interleukin 6.[44,51]

4 | APPLICATIONS OF TES FOR GI TRACT MOTILITY

The use of TES in GI motility has shown promising results. Treatments are usually well tolerated and can be self-administrated safely at home. For instance, studies with tcVNS and IFC can be performed via a handheld device over the anterior neck.[8,52,53] Additionally, studies with TEA on acupuncture points of PC6 and or ST36 showed good compliance with a wearable device and found that TEA improved symptoms of GERD,[34,35] FD,[33] and gastroparesis.[33,35,54] No side effects were noted in these studies.[55] Generally, the results of TES lead to rapid improvement in symptoms shortly after treatment.[44] However, beneficial effects of IFC stimulation are reported to start relatively slower but last a longer duration (about 0.5–2 years) even after cessation of the stimulation.[42]

5 | ESOPHAGEAL MOTILITY DISORDERS

Esophageal motility disorders could manifest with various symptoms, including dysphagia, heartburn, and regurgitation.[56,57] Treatment of esophageal motility disorders has been challenging because of the lack of effective prokinetic agents and a high rate of refractoriness to certain medications, such as acid antisecretory drugs. However, TES has been studied as a potential treatment option for managing some of these disorders. Techniques studied involve TENS, TEA, and IFC (Table 1).

5.1 | Dysphagia

Dysphagia is a common GI symptom defined as an abnormality in the passage of solids or liquids from the oral cavity to the stomach, possibly associated with various oropharyngeal and esophageal motor or sensory disorders.[58,59] Currently, TES (such as IFC and TENS) is one of the several tools available to improve swallowing muscle function and treat various types of dysphagia.[60] Electrodes are usually placed in the anterior neck in two regions, the upper region between the mandibula and hyoid bone and the lower region below the hyoid bone.[48]

Interferential current through the neck has been investigated and found safe and promising as an alternative treatment for patients with dysphagia (Table 1).[53,61–64] Afferent nerves are stimulated without causing muscle contractions by using this method.[61]

TABLE 1 Transcutaneous electrical stimulation (TES) on esophageal motility disorders.

References	Disease	Technique	Study design	Stimulation location	# of subjects	TES regimen	Outcome measures	Findings
Yuan et al.[52]	Dysphagia	tcVNS	Case report	Right cervical nerve stimulation	1	20 min/day 5 days/week 6 weeks	Swallow symptoms and barium swallow	Improvement in swallowing function and decrease in saliva spitting
Oku et al.[63]	Refractorydysphagia	IFC	Cohort study	Anterior neck	12	15 min Acute IFC	Videofluoroscopy to measure the sensory threshold on swallowing reflex	Shortened the pharyngeal response duration and increased the number of swallows
Maeda et al.[64]	Dysphagia	IFC	RCT	Anterior neck	43	15 min twice per day for 2 weeks	Cough latency time, functional oral intake scale, and oral nutrition intake	Improvement in cough latency time and oral nutrition intake
Sun et al.[65]	Dysphagia	TENS	Meta-analysis	Anterior neck	585	30–70 min/day	Swallowing function scale	Improvement in the Swallowing Function Scale scores
Zou et al.[103]	Healthy volunteer	TENS	RCT	PC6	14	60 min Acute TENS	Symptoms TLESRs (measured by esophageal manometry	Inhibition in the frequency of TLESR
Hu et al.[46]	GERD	TEA	RCT	PC6 and ST36	30	30 min Acute TEA	Symptoms Esophageal manometry Gastric accommodation HRV	Improvement in symptoms, esophageal manometry, gastric accommodation, and vagal activity
Liu et al.[77]	GERD	STEA	RCT	ST36	60	30 min	Esophageal manometry HRV	Increased LESP and vagal activity
Meng et al.[34]	RefractoryGERD	TEA	RCT	PC6 and ST36	20	30 min twice daily	GERDQ Esophageal manometry	Increased GERDQ and LESP

TABLE 2 Transcutaneous electrical stimulation on gastric motility disorders.

References	Disease	Technique	Study design	Stimulation location	# of subjects	TES regimen	Outcome measures	Findings
Sukasem et al.[9]	Healthy porcine model	taVNS	Randomized and sham-controlled	Anthelix of the left ear	9	10 min Acute taVNS	Gastric slow waves via serosal implanted electrodes	taVNS at 10 Hz normalized gastric slow wave, and 80 Hz inhibited gastric slow waves
Gottfriend-Blackmore[8]	Idiopathic gastroparesis	taVNS	Open label	Lateral neck (cervical vagal nerve)	15	Twice daily 4 weeks	Symptoms Gastric emptying Vagal activity by HRV	Improvement in symptoms and gastric emptying
Kaut et al.[79]	Gastroparesis symptoms in Parkinson's patients	tcVNS	Cohort study	Lateral neck (cervical vagal nerve)	19	Four times daily 4 weeks	Symptoms Gastric emptying using a ^{13}C-octanoic acid breath test.	Improved symptoms. No difference in gastric emptying
Huang et al.[23]	Healthy volunteers (with a cold liquid challenge)	TEA	RCT	PC6 and ST36.	13	30 min Acute TEA	Gastric accommodation Gastric slow waves by EGG and vagal activity by HRV	Improved gastric accommodation, gastric slow waves, and vagal activity
Song et al.[47]	Idiopathic Gastroparesis	STEA	RCT	PC6 and ST36	18	60 min Acute STEA	Symptoms Gastric slow waves by EGG Vagal activity by HRV	Decreased nausea scores Enhanced vagal activity
Sarosiek et al.[31]	Diabetic Gastroparesis	TEA	RCT	PC6 and ST36.	11	60 min Acute TEA	Gastric slow waves by EGG Brain activity by EEG	Improved nausea and gastric slow waves, associated with a change in the dominance of right to left frontal lobe activity
Weinkauf et al.[81]	Gastroparesis post lung transplant	TENS	Case reports	Thoracic region	2	30 min daily 19–21 days	Symptoms Ability to tolerate a diet Weight gain	Resolution of symptoms, tolerance of diet, and weight gain
Frokjaer et al.[16]	Dyspepsia	taVNS with deep slow breathing	Cohort study	Left concha (Auricular branch of the vagus nerve)	18	60 min Acute taVNS	Cardiac autonomic testing, conditioned pain modulation, and liquid meal gastroduodenal motility test	Increased cardiac vagal tone, bone pain thresholds, frequency of antral contraction, and gastroduodenal motility index
Xu et al.[55]	Functional dyspepsia Health volunteers	TEA	RCT	ST36 and PC6	8 8	30 min Acute TEA	Gastric accommodation assessed by nutrient drink Gastric slow waves by EGG	Improved gastric accommodation and the percentage of normal gastric slow waves
Liu et al.[82]	Functional dyspepsia	TEA	RCT	PC6 and ST36	27	30–60 min Two times daily 2 weeks	Symptoms, gastric slow waves by EGG, vagal activity by HRV, neuropeptide Y (NPY), and motilin	Improvement in dyspepsia, vagal activity, percentage of normal gastric slow waves, and plasma levels of NPY. However no change in motilin
Ji et al.[33]	Functional dyspepsia	TEA	RCT	PC6 and ST36	28	60 min daily 2 weeks	Symptoms Gastric accommodation Gastric emptying Gastric slow waves by EGG	Improvement in dyspepsia symptoms, gastric accommodation, gastric emptying, and gastric slow waves

TABLE 2 (Continued)

References	Disease	Technique	Study design	Stimulation location	# of subjects	TES regimen	Outcome measures	Findings
Ma et al.[32]	Healthy volunteer	STEA	RCT	PC6	15	45 min Acute TEA	Symptoms Gastric accommodation Gastric slow waves by EGG Vagal activity by HRV	STEA is superior to TEA in improving dyspepsia, gastric accommodation, gastric dysrhythmia, and vagal activity
Köklü et al.[84]	Dyspepsia	IFC	RCT	Thoracic vertebra 10–12	44	Twelve 15-min sessions for 4 weeks	Self-reported change in dyspepsia symptoms	Improvement in dyspepsia symptom

Abbreviations: GCSI, gastroparesis cardinal symptom index daily diary; RCT, randomized control trial.

An animal study has shown that IFC through the neck could augment the sensory afferent pathways and improve the swallowing reflex.[62] A cohort study by Oku et al.[63] has demonstrated that IFC significantly shortened the pharyngeal response duration from 0.72 to 0.64 s in dysphagic patients and increased the number of swallows ($p < 0.035$). A randomized controlled trial using IFC versus the sham stimulation for 2 weeks[64] showed significant improvement in cough latency time and oral nutrition intake in 43 dysphagia patients. However, the sham stimulation was set at a low intensity of 0.1 mA compared to 3.0 mA in the IFC group, likely not causing any sensation typically experienced with actual IFC.

Transcutaneous electrical nerve stimulation via neck has also been studied as a potential therapeutic method for swallow dysfunction.[65–72] A recent meta-analysis of eight randomized controlled trials and three clinical controlled trials assessed 585 patients with dysphagia who received either TENS or sham for their dysphagia.[65] The study demonstrated TENS could significantly improve swallowing function in patients with acquired brain injury. The effectiveness of TENS was also demonstrated by stimulating the suprahyoid and infrahyoid muscle groups or by stimulating the infrahyoid muscle groups, especially with a stimulation session of up to 45 min or less.

Transcutaneous cervical vagal nerve stimulation is scarcely studied for dysphagia and was only recently reported in a case report,[52] which found improvement in swallowing function after a 6 week of 20-min daily tcVNS treatment.

5.2 | Gastroesophageal reflux disease

Gastroesophageal reflux disease (GERD) is one of the most common GI disorders. Current treatment approach that includes weight loss, lifestyle modification, and anti-reflux medications still fall short of complete relief of symptoms. Lower esophageal sphincter (LES) dysfunction plays an important role in pathological mechanisms of reflux.[73] LES electric stimulation therapy gained attention due to effective control of esophageal acid exposure and amelioration of reflux symptoms.[74,75] However, the technique was abandoned in the United States because of its invasiveness of this approach and lack of long-term effectiveness.

Needleless TEA was recently evaluated as an alternative therapeutic approach for LES dysfunction in several studies (Table 1).[34,35,46,76,77] A randomized controlled trial by Meng et al.[34] has shown that TEA significantly improved GERD symptoms and LES pressure (by 52.2%) after the TEA treatment compared to the sham stimulation ($t = 5.91$, $p = 0.004$) in 20 refractory GERD patients. Hu et al.[46] reported a significant reduction in postprandial fullness and improvement in gastric accommodation, gastric slow waves, and vagal activity in GERD patients treated with TEA compared to sham stimulation. A randomized controlled trial aimed to determine the effect of 4-week TEA or sham stimulation combined with deep breathing training (DBT) in 20 refractory GERD patients. The authors showed that the combination of TEA with DBT was significantly more effective in decreasing reflux symptom scores than sham TEA

TABLE 3 Transcutaneous electrical stimulation on small and large intestinal motility disorders.

References	Disease	Technique	Study design	Stimulation location	# of subjects	TES regimen	Outcome measures	Findings
Venara et al.[20]	Post-op ileus (patients underwent elective colectomy)	tTNS	Patient-blinded RCT	Behind internal malleolus	15 with tTNS 19 with sham	20 min, the day before surgery, and on the day of surgery, post-op three times daily until GI motility recovered	Delay in GI motility recovery: passage of stool and tolerance of solid food	No difference in GI motility recovery between both groups. However, occurrence of post-op ileus was higher in placebo group in per-protocol analysis
Hong et al.[86]	Post-op ileus (patients underwent open laparotomy)	tVNS	Open-label	Cymbal conchae of the right ear	14	10-min intraoperatively	Gastric EMG Gastrin levels	Reduction of gastric action potential frequency, increase of amplitude, and increase of Gastrin levels
Zhang et al.[37]	Post-op ileus (patients underwent abdominal surgical removal of GI cancer)	TEA	RCT	ST36 and PC6	21 with TEA 21 with sham	60 min/session Two sessions daily from post-op Days 1–3	Time to defecation and resume diet, ambulation, pain score; vagal activity by HRV, and inflammatory markers	Improved post-op symptoms, increased vagal activity, decreased inflammatory markers
Iqbal et al.[12]	Chronic functional constipation	tSNS	Open-label	Sacrum	16	30 min daily 6 weeks	Constipation symptoms	Ineffective for chronic constipation
Iqbal et al.[11]	Chronic functional constipation	tTNS	Open-label	Posterior to medial malleolus	12	30 min daily 6 weeks	Constipation symptom	Improved quality of life, however, no constipation symptoms
Gokce et al.[21]	Chronic functional constipation	tTNS	RCT	Below and above medial malleolus	22	20 min/sessions Three sessions/week 6 weeks	Constipation symptoms at 6 weeks and 12 weeks	Improved constipation symptoms during the tTNS, and the effect continued for 12 weeks after the treatment
Liu et al.[88]	Ischemic stroke-induced constipation	TEA	RCT	ST36	43 with TEA 32 with sham	60 min/session Two sessions daily 2 weeks	Constipation symptoms Vagal activity by HRV	Increased BMs, decreased straining, reduced laxative use. Increased vagal activity
Chase et al.[40]	Chronic constipation (pediatric patients)	IFC	Pilot study-open label	Paraspinal area of T9-L2; anterior abdominal wall below the costal margin	8	20 min/session Three sessions weekly 3–4 weeks	Daily bowel diary before, during 1 and 3 months after treatment	Stopped soiling in 87.5% of children and increased stool frequency. Effect last for 3 months in 50% of patients
Clarke et al.[90]	Slow transit constipation (pediatric patients)	IFC	RCT	Paraspinal area of T9-L2; anterior abdominal wall below the costal margin	26	20 min/session Three sessions weekly 4 weeks	Nuclear colonic transit studies	Improved nuclear transit time

TABLE 3 (Continued)

References	Disease	Technique	Study design	Stimulation location	# of subjects	TES regimen	Outcome measures	Findings
Clarke et al.[89]	Slow transit constipation (pediatric patients)	IFC	RCT	Paraspinal area of T9-L2; anterior abdominal wall below the costal margin	16 with IFC 17 with sham	20 min/session Three sessions weekly 4 weeks	QoL, Holschneider and Templeton scores	Improved QOL, Holschneider score. No change in Templeton scores
Ismail et al.[91]	Slow transit constipation (pediatric patients)	IFC	Open-label	Paraspinal area of T9-L2; anterior abdominal wall below the costal margin	11	60 min daily 1 month	Bowel diary	Increased defecation but not soiling
Leong et al.[92]	Slow transit constipation (pediatric patients)	IFC	RCT	Paraspinal area of T9-L2; anterior abdominal wall below the costal margin	39	15–30 min/session Three sessions weekly 4–8 weeks	Constipation symptoms follow-up for an average of 3.5 years	33% of patients have lasting improvement for more than 2 years
Yik et al.[93]	Slow transit constipation with concurrent upper GI dysmotility (pediatric patients)	IFC	RCT	Paraspinal area of T9-L2; anterior abdominal wall below the costal margin	46	20 min/session Three sessions weekly 4 weeks	Nuclear colonic transit studies	Transit time improved after 2 months with normal upper GI motility, not in concurrent upper GI dysmotility group
Yik et al.[94]	Slow transit constipation (pediatric patients)	IFC	Open-label	Paraspinal area of T9-L2; anterior abdominal wall at the level of the umbilicus	32	60 min daily 3–6 months	Bowel diaries, Peds PAC-QoL, nuclear colonic transit studies	Improved BMs, soiling, and QoL Improved colonic transit in 13/25 patients
Queralto et al.[39]	Slow transit constipation	IFC	Open-label	Paraspinal area of T9-L2; anterior abdominal wall below the costal margin	11	60 min daily 3 months	Stool diary, Knowles-Eccersley-Scott symptom score, CCC score, PAC-QoL; colonic transit studies	IFT improved stool frequency, QoL, and decrease KESS score and CCC score. Improved transit time
Clarke et al.[95]	Slow transit constipation (pediatric patients)	IFC	Open-label	Paraspinal area of T9-L2; anterior abdominal wall below the costal margin	8 children	20 min/session three sessions weekly 4 weeks	Colonic manometry before, 2 and 7 months after tx	IFC increased propagating sequences, effect last for 2–7 months
Yang et al.[83]	Slow transit constipati on (Female)	IFC	RCT	Paraspinal area of T9-L2; anterior abdominal wall below the costal margin	14 with IFC 14 with sham	20 min/session three sessions weekly 4 weeks	CAS, abdominal pain # BM weekly	Increased BM weekly with IFC. Decreased CAS score and abdominal pain in both IFC and sham

(Continues)

TABLE 3 (Continued)

References	Disease	Technique	Study design	Stimulation location	# of subjects	TES regimen	Outcome measures	Findings
Moore et al.[38]	Chronic functional constipation (Female)	IFC	RCT- patient blinded	Paraspinal area of T9-L2; anterior abdominal wall below the costal margin	23 with IFT 22 with sham	60 min daily 6 weeks	Bowel diary, PAC-SYM, PAC-QoL, nuclear colonic transit studies, and anorectal manometry	Increased bowel frequency in 53% compared with sham. Reduce PAC-SYM, overall symptoms, less laxative use in IFC group. Effects last for at least 3 months
Coban et al.[97]	IBS	IFC	Double-blinded RCT	Paraspinal area of T9-L2; anterior abdominal wall below the costal margin	29 with IFC 29 with sham	15 min/session Three sessions weekly 4 weeks	IBS global assessment of improvement scale, QoL, numeric rating scales, visual analogue scale	Improvement of symptoms during treatment. Symptoms continued to improve for 1 month after stopping the IFC
Xiao et al.[98]	IBS-D IBS-C Functional constipation	TEA	Open-label	Acupuncture points HI4, ST36, and UB 57	24 IBS-D 20 IBS-C 30 functional constipation	30 min/session Twice weekly 2 months	Bowel diary and rectal sensory thresholds. abdominal pain	Improvement of rectal sensory thresholds in IBS-D with TEA but not in IBS-C or FC. Improvement of BM frequency and abdominal pain in IBS-D
Zhou et al.[99]	IBS-C	TEA	RCT	Acupuncture point ST36	22 with TEA 22 with sham	60 min/session two sessions daily 2 weeks	Constipation symptoms, QoL, anorectal function by anorectal manometry, and vagal activity by HRV	Improvement of symptoms, rectal sensation, and vagal activity during TEA. Constipation symptom continued to improve for 1 month after cessation of the TEA
Xiao et al.[100]	Functional constipation	TEA	Phase I: Acute TEA Phase II: A crossover design	Acupuncture points ST36	53 in the acute phase 18 in the crossover phase	30 min/session two sessions daily 2 weeks	Constipation symptoms and rectal sensory thresholds. abdominal pain	Improvement of BM frequency, rectal sensation, and vagal activity
Huang et al.[101]	IBS-C	TEA	RCT	Acupuncture point ST36	26 with TEA 26 with sham	60 min/session two sessions daily 4 weeks	Constipation symptoms, QoL, VAS pain score, colonic transit by radiopaque maker, rectal sensation by anorectal manometry, and vagal activity by HRV.	Improvement of symptoms, rectal sensation, colonic transit, and vagal activity

Abbreviations: CAS, constipation assessment scale; CCC, Cleveland clinic constipation score; PAC-QoL, patient assessment of constipation quality of life; PAC-SYM, patient assessment of constipation symptoms; TEA, transcutaneous electrical acustimulation; tSNS, transcutaneous sacral nerve stimulation; tTNS, transcutaneous tibial nerve stimulation; tVNS, transcutaneous vagus nerve stimulation; VAS, visual analogue scale.

with DBT.[35] More recently, synchronized TEA (STEA) has emerged as a novel technique that consists of the delivery of a TEA stimulus in synchronization with inspiration and has been found to further enhance autonomic function, compared to TEA without synchronization in breathing.[76] A study by Liu et al.[77] has shown that acute STEA increased vagal activity and LES pressure in GERD patients compared to sham STEA. These findings on TEA therapy for GERD are promising and suggest that the vagal effect on the lower esophageal sphincter may mediate the improvement in GERD symptoms.

Transcutaneous electrical stimulation techniques, such as IFC, TENS, and TEA therapy, target key aspects of esophageal motility disorders by stimulating afferent nerves,[61] enhancing swallowing reflexes,[62] improving esophageal and gastric motility,[46] and increasing LES pressure.[34,77] These improvements are primarily achieved through the modulation of PNS and SNS. By addressing these core components, TES offers alternative treatment options for patients with esophageal motility disorders, providing a more comprehensive approach to management.

6 | GASTRIC MOTILITY DISORDERS

Gastroparesis and FD are common gastric motility disorders, and symptoms usually include upper abdominal pain, early satiety, nausea, and vomiting. TES has been studied as an adjunct or an alternative therapy for these conditions (Table 2).[8,23,31,47,78,79]

6.1 | Gastroparesis

Gastroparesis is defined as delayed gastric emptying in the absence of mechanical obstruction.[8,54] The common etiologies of gastroparesis may include diabetes mellitus, surgery, viral illnesses, or opioids.[54] Gastroparesis can be debilitating. A mainstay of treatment includes lifestyle changes, antiemetics, prokinetic agents, and in rare instances, invasive surgical options.[8] TES has shown promising results in treating gastroparesis, particularly using tVNS, TEA, and TENS.

There are few human studies on gastroparesis and the use of tVNS.[8,79] Notably, In an open-label pilot cohort study, Gottfriend-Blackmore et al.[8] performed the first human study showing bilateral tcVNS-improved symptoms and gastric emptying in 15 patients with idiopathic gastroparesis. In another randomized controlled clinical trial, Kaut et al. found a subjective improvement in symptoms in the treatment group ($n=10$) without statistically significant, and there was no difference in the gastric emptying measured by the ^{13}C-octanoic acid breath test in 19 patients with Parkinson's disease that suffered from gastroenteric complaints similar to gastroparesis.[79] The insignificant results were likely due to small sample size, nonspecific GI complaints without a diagnosis, and the day-to-day variation of a breath test for gastric emptying was about 30%.

Transcutaneous electrical acustimulation treatment in patients with gastroparesis improved overall nausea and vomiting, gastric dysrhythmia, and vagal activity.[23,31,47] Huang et al.[23] demonstrated that TEA (compared to sham stimulation) improved impaired gastric accommodation (731.0 ± 185.7 vs. 539.2 ± 133.8 mL, $p=0.005$) and increased the percentage of normal gastric slow waves ($p<0.05$) in 13 healthy volunteers consuming a cold liquid challenge. Similarly, a study by Song et al.[47] found that in patients with idiopathic gastroparesis, there was a 38% reduction in nausea symptom score, a 24% increase in the percentage of normal gastric waves, and a threefold increase in vagal activity after liquid meal challenge in those receiving TEA synchronized with breathing compared to sham stimulation ($p<0.05$). Sarosiek et al.[31] further looked into the mechanisms of TEA by using electroencephalography and electrogastrography measurements to assess central and peripheral responses during TEA in patients with diabetic gastroparesis. They found that during initial visual stimulation that provoked nausea, the right inferior frontal activity was dominant, and when TEA was performed, the left inferior frontal activity was dominant. The left inferior frontal lobe activity has been associated with experiencing pleasant stimuli.[31,80] The authors also found that the visual stimulation that provoked nausea was associated with a decrease in the percentage of normal gastric slow waves. When TEA was added, there was an improvement in gastric slow waves. These findings support the idea that the autonomic and central nervous systems play a key role in the mechanism of TEA.

There is a limited number of studies using TENS in gastroparesis. Only case reports are currently available. Weinkauf et al.[81] reported TENS improved the symptoms in two patients who developed severe gastroparesis after lung transplants for advanced cystic fibrosis. While results from these case reports appear promising, sham-controlled clinical trials are needed to validate these data.

6.2 | Functional dyspepsia

Dyspepsia is defined as a cluster of symptoms that originate from the gastroduodenum.[33,35,82] Symptoms include upper abdominal pain, early satiety, nausea, vomiting, and bloating. Some key pathophysiological factors of FD are thought to be caused by increased visceral sensitivity, impaired gastric accommodation, and delayed gastric emptying.[33,82] Pharmacotherapy varies in effectiveness and includes antacids, prokinetic agents, and anti-depressants.[82] Acupuncture has been used to treat FD, and TES has become a potential treatment of interest for FD, particularly in the forms of taVNS, TEA, and IFC.

Frøkjaer et al.[82] investigated taVNS effects on musculoskeletal pain and gastroduodenal motility in a randomized, sham-controlled, crossover study with 18 healthy subjects. The treatment group experienced increased cardiac vagal tone, bone pain thresholds, antral contraction frequency, and gastroduodenal motility index. However, the study's limitations include assessing only healthy individuals and a short treatment duration.

Several studies have demonstrated the effectiveness of TEA in treating FD.[32,33,55,82] In a pilot study by Xu et al., TEA at acupuncture points PC6 and ST36 improved dyspepsia symptoms, gastric accommodation, percentage and power of the normal gastric waves in the fed state, and increased vagal activity in patients with FD.[55] Liu et al.[82] conducted a double-blind crossover study on 27 FD

patients. evaluating acute and chronic TEA effects. Acute TEA increased vagal activity by 76% but did not change gastric slow waves. Two-week TEA decreased dyspepsia symptoms by 55%, increased vagal activity by 75%, elevated serum NPY, but did not affect motilin levels. These results suggest TEA improves FD symptoms through vagal pathway modulation and GI hormones like NPY. Ji et al.[33] also performed a 2-week crossover clinical trial and found that TEA significantly improved dyspeptic symptoms, quality of life, gastric accommodation, and gastric emptying in 28 FD patients, compared to the sham stimulation. In another study using TEA synchronized with breathing, Ma et al.[32] showed that STEA is superior to TEA without synchronization in treating dyspepsia symptoms. Overall, these studies favor the use of TEA for the treatment of dyspepsia. Adding synchronization in breathing to TEA should be considered, as it has shown to superior efficacy than TEA. The mechanism is likely through its augmentation of parasympathetic activity.[83]

Studies using IFC in FD are limited. The only study to our knowledge is by KÖKLÜ et al., who used IFC over thoracic 10–12 in patients with FD.[84] The study showed improvement in dyspepsia symptoms compared to the control group. Future controlled studies are needed that measure objective data to validate the use of IFC in FD patients.

7 | POSTOPERATIVE ILEUS

Postoperative ileus (POI) remains one of the most common complications following intra-abdominal surgeries. It is associated with nausea, vomiting, abdominal distention, and delayed passage of flatus or stool due to transient episodes of impaired GI motility, leading to a prolonged hospital stay.[85] TES is a potential nonpharmacological approach for the treatment of POI, and current studies demonstrate its efficacy in improving postoperative GI symptoms.[37,86] Three studies were identified from a literature search that explored the effects of TES on POI (Table 3).[20,37,86] Techniques employed in these studies include taVNS, TEA, and tTNS.

taVNS was explored as a potential treatment option for 14 patients undergoing open laparotomy.[86] Each patient received 10 min of taVNS intraoperatively. taVNS decreased gastric action potential frequency (from 3.69 to 2.98 per min, $p < 0.05$) and increased action potential amplitude (from 0. 19 to 0.25 mV $p < 0.05$), with a 60% increase of gastrin levels after 3 h ($p < 0.05$). Further study will be needed to assess the effects of taVNS in preventing POI.

Transcutaneous electrical acustimulation was studied in a single-blinded randomized controlled trial that evaluated its effects on POI.[37] Forty-two patients undergoing abdominal surgical removal of GI cancer were recruited and divided into the TEA group and the sham stimulation group. Both groups received a 1-hour session of treatment twice a day from the postoperative day (POD) 1–3. TEA improved major postoperative symptoms by 30%, including a shorter time to first bowel movement, passing flatus, ambulation, and initiation of a diet, compared to sham stimulation. These effects were associated with enhanced vagal activity and reduced serum norepinephrine level.

tTNS was also studied in treating POI in a pilot randomized controlled trial.[20] Patients undergoing elective colectomy were recruited. A total of 15 patients received tTNS, and 19 patients received sham stimulation. Each stimulation session last 20 min. One session daily for the day before surgery and on the day of surgery, and three sessions daily postoperatively until recovery of GI motility. Overall, there was no difference in GI motility recovery between both groups in the intention-to-treat analysis. However, in the per-protocol analysis, the occurrence of POI was higher in the sham stimulation group compared with the tTNS group.

8 | COLONIC MOTILITY DISORDERS

8.1 | Constipation

Chronic constipation is one of the most common GI disorders that significantly impacts the quality of life and is associated with a substantial financial burden to the healthcare system. Apart from chronic constipation that a systemic disease or organic causes could explain, most cases are idiopathic.[87] Treatment of constipation remains a challenge, despite many pharmacological agents. TES is one of the alternative therapeutic options that has been extensively explored in treating constipation, including IFC, TEA, tTNS, and tSNS (Table 3). Overall, studies support the value of TES in treating constipation, thus making it a potential option in treating constipation.[11,12,21,38,39,40,83,88–95]

In an early study, IFC delivered by a therapist resulted in an 87.5% increase in bowel movement frequency, and the effect lasted for 3 months in 50% of pediatric patients with chronic constipation.[40] Subsequent randomized controlled studies assessed the effects of 4-week IFC versus the sham stimulation on slow transit constipation in 26 children and demonstrated that IFC but not the sham stimulation shortened colonic transit time.[90] Colonic propagating sequences were also studied in eight children and were found to be increased by IFC (78 vs. 210 propagating sequences/24 h, $p = 0.008$), and the effect lasted for at least 2–7 months.[95] Recently, a few home-based self-administered IFC showed similar effects as the therapist-administered IFC to increase bowel movement frequency,[91] colonic transit, and quality of life in pediatric patients.[94]

There are fewer studies regarding the application of IFC in treating adult constipation. The first published study in 2012 reported 11 adults with slow transit constipation who received 1-hour daily treatment at home for more than 3 months. IFC treatment was shown to improve stool frequency per week (0.66 vs. 1.66, $p = 0.007$), decrease Knowles-Eccersley-Scott Symptom score (30 vs. 19, $p = 0.005$), Cleveland clinic constipation score (26 vs. 17, $p = 0.005$), improved colonic transit time (103 vs. 98 h, $p = 0.02$), and QoL score (60 vs. 95, $p = 0.005$).[39] An assessor-blinded, randomized controlled trial applied IFC to women with slow transit constipation. Twenty-eight women were divided into treatment and control groups. A trained therapist gave 20 min treatment a day, three times a week for 4 weeks. There was a decrease in constipation assessment scale score and abdominal pain in both IFC and sham group; however, an increase in defecation per week was only observed in the IFC group ($p < 0.05$).[83] In a recent study, 45 women were divided

into IFC and sham groups. Patients were trained to self-administer treatment 1 h daily for 6 weeks. Bowel frequency increased in 53% of patients compared with sham (53% vs. 12%, $p=0.02$) along with reduction of PAC-SYM ($p=0.03$), overall symptoms ($p=0.05$), and laxative use in the IFC group ($p=0.01$).[38] The effects lasted for at least 3 months. Therefore, IFC seemed a promising treatment option for adults with slow transit constipation.

Transcutaneous electrical acustimulation was assessed as a potential treatment for ischemic stroke-induced constipation in a randomized, patient-blinded, sham-controlled trial.[88] Forty-three patients received TEA at acupoint ST36, while 32 received sham TEA. After 2 weeks, TEA significantly decreased the incidence of stroke-induced constipation (68.2 vs. 42.9%, $p=0.029$), increased weekly bowel movements (4.5 vs. 5.5, $p=0.001$), improved stool consistency and quality of life ($p<0.05$), and modulated vagal and sympathetic activity (as measured by HRV). These results suggest TEA could be a potential therapy for constipation.

A pilot study was conducted using tSNS to treat 16 adult patients with chronic functional constipation.[12] Two surface electrode pads were applied along both sides of the sacrum. Every patient received self-administration tSNS daily for 4 weeks at home. There was no significant change in outcome measures of constipation in patients receiving tSNS. However, this study was limited by a small sample size.

tTNS was explored in two studies as a potential treatment option for chronic functional constipation.[11,21] In a pilot study,[11] 12 adult patients completed self-administration of bilateral tTNS 30 min daily over a period of 6 weeks. Only the quality of life score improved (2.95 vs. 2.50, $p=0.047$) without significant changes in symptoms of constipation. In another prospective study, 44 geriatric patients received 20 min tTNS session three times a week for a period of 6 weeks that was administered by a therapist. Overall, there was an improvement in constipation severity at the end of treatment measured by time spent in the toilet. In addition, 47.7% of patients reported a decrease in stool softeners, and the effects lasted for at least 12 weeks after treatment.[21]

8.2 | Irritable bowel syndrome

Irritable bowel syndrome is a common functional GI disorder that greatly affects quality of life and is characterized by chronic, recurrent abdominal pain, or discomfort associated with altered bowel habits.[96] The treatment for IBS has remained a great challenge, involving lifestyle modifications and pharmacological agents based on predominant symptoms. TES is a potential treatment option for managing IBS,[97,98] and techniques identified in those studies include IFC, TEA, and taVNS.

A prospective double-blinded randomized controlled trial studied the application of IFC as a possible treatment for IBS. Fifty-eight adults with IBS were randomly assigned to IFC treatment and sham. Both groups received 12 sessions of 15 min actual IFC versus sham IFC treatment during 4 weeks. This study demonstrated improvement of IBS symptoms in both IFC and placebo groups; however, the severity of IBS symptoms ($p<0.02$) and visual analog scores ($p<0.001$) continued to improve over 1 month after treatment in the IFC treatment group.[97] Also, IFC was able to significantly improve the quality of life score (from 93 to 77.9, $p=0.014$). Therefore, IFC could be a useful treatment option for IBS, but further studies are needed.

A pilot study published in 2004 explored the application of TEA in managing diarrhea-predominant IBS (IBS-D)[98] and provided evidence for the potential value of TEA in improving abdominal pain and rectal sensation in patients with IBS-D (Table 3). Several recent trials on TEA have shown that 2-week TEA ameliorated constipation and enhanced vagal activity in patients with constipation-predominant IBS (IBS-C)[99] and functional constipation.[100] The improvement of constipation can be sustained 4 weeks after cessation of the TEA treatment.[99] In another recent trial,[101] 52 patients were randomized into TEA and sham groups. TEA was superior to sham in improving IBS-C by promoting colon transit and decreasing rectal sensation through the vagal pathway. Further studies are needed to establish the long-term value of TEA in IBS.

In a study[102] examining the effects of taVNS on IBS, Mion et al. evaluated twelve female IBS patients undergoing taVNS treatment for 6 months. The assessment considered symptom improvement, feasibility, and various physiological and biological variables. Nine patients completed the trial, showing significant IBS symptom relief at 3 and 6 months; however, taVNS did not alter any of the measured variables. These preliminary findings indicate that taVNS may be a feasible and effective intervention for IBS, necessitating further investigation through randomized controlled trials.

9 | CONCLUSIONS

In this review, we have introduced the methodology of TES, summarized the mechanisms of action of TES, and provided an overview of TES effects in animal models and patients with GI motility disorders. Overall, needleless TES is a safe, noninvasive, home-based, and self-administrative technique. In the majority of cases, the treatment protocol requires application once or twice daily, with each treatment session lasting up to 60 min. Based on the collective evidence derived from studies published to date, TES has a potential role as an alternative or adjunctive therapy for the management of the mentioned disorders and related symptoms involving different segments of the gut.

Further studies are needed to better define TES efficacy, especially given the heterogeneous, multifactorial aspects, chronicity, and high placebo response of these disorders. Long-term randomized controlled trials are needed to validate the chronic effects of TEA. Furthermore, it is essential to optimize TES methodology, study design, and outcome measurements. We are at a pivotal moment in medical history, with the golden opportunity to fully unleash the therapeutic prowess of TES in the management of GI motility disorders.

AUTHOR CONTRIBUTIONS

GS: conceptualization, investigation, data curation, visualization, drafting, editing manuscript. ST, YF, FS: data curation, visualization,

drafting manuscript. JC: editing manuscript. RF: editing manuscript. GS will serve as the guarantor, ensuring the integrity of this work in its entirety, from inception to publication. All Authors have approved the final version of the manuscript.

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