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Effects of transcutaneous auricular vagus nerve stimulation added to robotic rehabilitation in patients with ischemic stroke: a randomized clinical trial

Ömer Dicle Kızıl[1,6], İbrahim Halil Ural[2], Sefa Haktan Hatık[3*], Ali Veysel Özden[4] and Emine Büşra Aydın[5]

Abstract

Background This study aimed to investigate the effects of adding transcutaneous auricular vagus nerve stimulation (taVNS) to robotic rehabilitation on functional outcomes and neuromuscular activity in patients with ischemic stroke.

Methods This randomized controlled clinical trial employed a pre–post study design and was conducted in a hospital-based physiotherapy and rehabilitation clinic. A total of 40 patients with ischemic stroke, aged 18–65 years, were randomly assigned to either a robotic rehabilitation group (RRG) or a combined vagus nerve stimulation and robotic rehabilitation group (VRRG). Spasticity, walking speed, motor function, quality of life, muscle activity, and pain were assessed at baseline and after six weeks of treatment.

Results Primary outcome measures were walking speed, motor function assessed by the Fugl–Meyer Assessment, and pain intensity. Secondary outcomes included electrophysiological measurements (H-reflex and F-wave parameters) and quality of life. Within-group analyses showed significant improvements in all outcomes in the VRRG ($p < 0.05$), whereas all outcomes except pain improved significantly in the RRG ($p < 0.05$). Between-group comparisons demonstrated greater improvements in walking speed in the VRRG compared with the RRG (mean difference − 1.84 s, 95% CI − 3.7 to − 0.7; $r = 0.43$; $p = 0.006$) and greater pain reduction in the VRRG (mean difference − 1.55, 95% CI − 2.5 to − 0.1; $r = 0.30$; $p = 0.048$). In contrast, a greater reduction in the Hmax/Mmax amplitude ratio—an electrophysiological marker of spinal excitability—was observed in the RRG.

Conclusion The findings suggest that transcutaneous auricular vagus nerve stimulation combined with robotic rehabilitation may provide additional benefits in terms of walking speed and pain reduction in patients with ischemic stroke.

Trial registration The study was registered at ClinicalTrials.gov on April 19, 2024. (Identifier: NCT06381089).

Keywords Stroke, Robotic rehabilitation, Vagus nerve stimulation

*Correspondence:
Sefa Haktan Hatık
haktanhtk@gmail.com; sefahatik@sinop.edu.tr
[1]Graduate Education Institute, Bahçeşehir University, Istanbul, Türkiye
[2]Department of Physical Medicine, Treatment and Rehabilitation, Faculty of Medicine, Beykent University, Istanbul, Türkiye
[3]Department of Health Care Services, Türkeli Vocational School, Sinop University, Sinop, Türkiye
[4]Department of Physiotherapy and Rehabilitation, Health Sciences Faculty, Bahçeşehir University, Istanbul, Türkiye
[5]Vocational School of Health Service, Gümüşhane University, Gümüşhane, Türkiye
[6]Haliç University, Istanbul, Türkiye

Introduction

Stroke represents a major global health burden and remains one of the leading causes of mortality and long-term disability worldwide. Recent estimates indicate that more than 12 million new stroke cases occur annually, with over 100 million stroke survivors globally, and the burden continues to increase with population aging, particularly in low- and middle-income countries, which account for nearly 70% of all stroke events [1, 2]. In Europe, stroke prevalence among adults is estimated to range between 1.5% and 2.5%, with markedly higher rates observed in older populations [3]. Stroke is defined by the World Health Organization as a clinical condition of vascular origin leading to focal or global impairment of brain function lasting longer than 24 h [4]. With the increasing elderly population, stroke has become more prevalent and is associated with a high risk of disability, frequently resulting in motor dysfunction and long-term functional limitations [5].

Post-stroke impairments may affect multiple components of physical function, including joint mobility and stability, muscle strength and tone, reflex activity, muscle endurance, motor control, and gait patterns, thereby restricting essential activities such as walking, balance, transfers, and postural control [6]. Motor impairment is the most common complication, with hemiplegia occurring in approximately 80% of patients, and a substantial proportion of survivors experiencing persistent functional deficits that significantly affect daily life [2]. Although advances in stroke treatment have led to a marked reduction in mortality, disability rates remain high, with more than 75% of survivors exhibiting residual impairments and up to 80% experiencing long-term sequelae [7]. In particular, walking difficulties following stroke substantially reduce independence and community participation, making the restoration of effective gait patterns and walking speed a primary goal of post-stroke rehabilitation [8, 9].

Despite advances in conventional post-stroke rehabilitation, recovery of independent walking remains challenging for many patients. Commonly used approaches—such as overground walking, treadmill training, body-weight–supported gait training, and therapist-assisted locomotor exercises—are often limited by therapist dependency, variability in training intensity, and insufficient high-repetition, task-specific practice, which may compromise motor learning. These limitations may restrict long-term improvements in walking speed and gait symmetry, particularly in patients with moderate motor impairment [6, 7].

Robot-assisted gait rehabilitation offers an important alternative to conventional approaches by providing repetitive, task-specific, and standardized locomotor training. Robot-assisted rehabilitation tools emphasize motor learning by requiring active engagement, effort, and attention from the patient, thereby facilitating the integration of robotic technologies into post-stroke clinical rehabilitation programs [10, 11]. However, although robotic gait rehabilitation supports motor learning, evidence suggests that when applied alone, functional gains may remain limited in some patients and neuroplastic responses may not be fully optimized [10–12].

Vagus nerve stimulation (VNS) refers to techniques that activate vagal afferent pathways and can be delivered either invasively via the cervical region or non-invasively through cervical or auricular stimulation [13]. Due to the potential risks associated with implanted devices, there has been growing interest in non-invasive vagus nerve stimulation techniques [14]. From a neurophysiological perspective, VNS may facilitate motor recovery by modulating cortical excitability, enhancing synaptic plasticity, and promoting activity-dependent motor learning through vagal afferent projections to brainstem nuclei and widespread cortical motor networks [15]. Experimental and clinical studies suggest that pairing VNS with task-specific motor training may strengthen sensorimotor integration and reinforce use-dependent plasticity, thereby augmenting rehabilitation-induced gains [16, 17].

Transcutaneous auricular vagus nerve stimulation (taVNS) has therefore gained increasing attention as an adjunctive neuromodulatory intervention in stroke rehabilitation. When combined with robotic gait training, which provides repetitive, task-oriented, and precisely controlled locomotor practice, taVNS may further enhance gait-related motor outcomes by supporting learning-dependent improvements in walking speed, coordination, and lower extremity motor control [18]. However, most existing taVNS studies in stroke rehabilitation have predominantly focused on upper-limb motor recovery, while evidence regarding lower-limb function and gait-related outcomes remains limited.

Accordingly, combining taVNS with robot-assisted gait rehabilitation represents a rational strategy to pair neuromodulation with task-specific locomotor training. The present study aimed to investigate the effects of adding taVNS to robotic rehabilitation on walking speed, lower-extremity motor function, pain, and neurophysiological parameters in patients with ischemic stroke [18, 19].

Methods

Design of the study

This study was conducted and reported in accordance with the CONSORT 2010 guidelines for randomized clinical trials. The trial followed a randomized clinical design with pre- and post-intervention assessments. The participant flow and study procedures are illustrated in detail in Fig. 1.

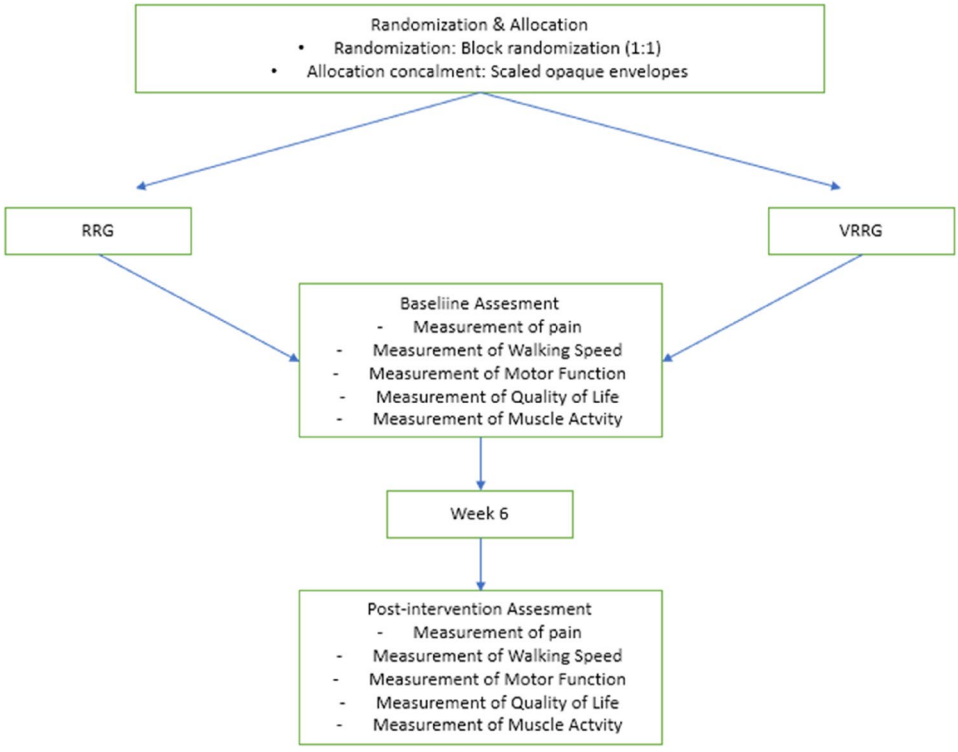

Fig. 1 Protocol of the study

Subject

40 patients over the age of 18 with ischemic stroke were the subjects of this study, which was carried out in the Istanbul Aydın University Medical Park Florya Hospital's Physical Therapy and Rehabilitation Unit and Robotic Rehabilitation Laboratory. Inclusion criteria: (1) have an ischemic stroke diagnosis; (2) have experienced a stroke for the first time; (3) have hemiparesis; (4) be within six months of the stroke; (5) be able to walk on their own or with assistance; (6) be able to comprehend and concentrate on Lokomat exercises; (7) have received training on walking with Lokomat at our hospital; (8) have signed the voluntary consent form; and (9) be older than eighteen. The study's exclusion criteria include: (1) body weight exceeding 135 kg; (2) height exceeding 2 m; (3) femur length exceeding 35–47 cm; (4) unacceptable leg length disparities; (5) peripheral nerve injury; (6) peripheral neuropathy; (7) anticholinergic medication use; (8) skin lesions; and (9) spasticity that impairs locomat function. (10) diagnosed mental health issues; (11) severe lower extremity muscle contracture; (12) stroke-related incapacity to walk; (13) history of other neurological conditions (e.g., Parkinson's disease); (14) unstable cardio-pulmonary disease; (15) orthopedic fractures (lower extremity fractures) and/or joint implants; (16) severe osteoporosis; (17) unstable cardio-pulmonary disease that is uncontrolled despite drug use; and (18) lower extremity amputation. Time since stroke was not analyzed as a separate baseline variable, as all participants were required to be within six months of their first ischemic stroke according to the inclusion criteria. All interventions ere performed by a physiotherapist with at least 5 years of experience.

To minimize potential confounding effects on electrophysiological outcomes, participants with conditions known to influence H-reflex and F-wave parameters—including peripheral neuropathy, diabetes mellitus–related neuropathy, lumbosacral radiculopathy, peripheral nerve injury, and other neurological disorders—were excluded based on medical history and clinical examination. All electrophysiological assessments were performed by an experienced neurologist using standardized protocols to ensure measurement consistency.

Out of the 45 individuals who underwent eligibility evaluation, one had severe osteoporosis, two had uncontrolled hypertension despite taking medication, and two declined to take part in the trial. Nevertheless, the study proceeded with 40 participants (Fig. 2). Following randomization, no participant left the trial for any reason.

Two groups were randomly selected based on the following data: age, gender, height, weight, body mass index, dominant side, affected side, and time since stroke. Participants were allocated into two groups: a combined Vagus Nerve Stimulation with Robotic Rehabilitation group (VRRG) ($n = 20$; 9 women, 11 men) and a Robotic

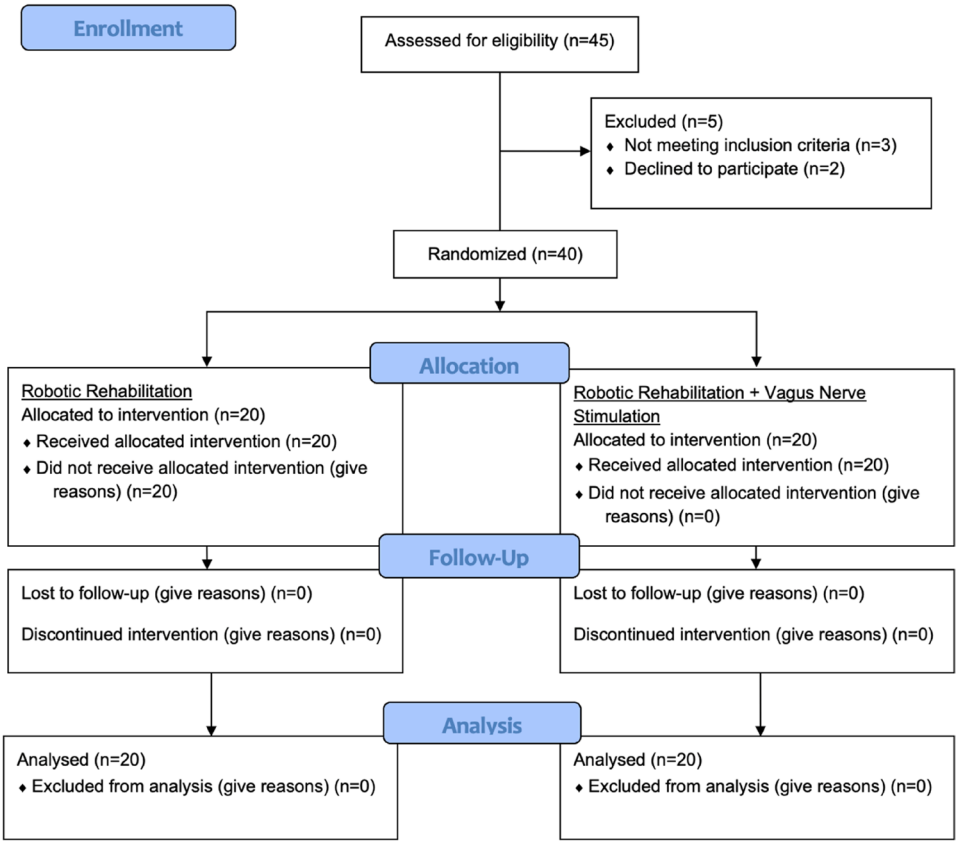

Fig. 2 CONSORT diagram

Rehabilitation–only group (RRG) ($n = 20$; 11 women, 9 men).

The investigation was conducted for six weeks in a quiet laboratory setting at Istanbul Aydın University Medical Park Florya Hospital, with the room temperature set at 25 ± 2oC one hour beforehand. Caffeine and alcohol use were restricted for participants at least 24 h in advance. The female subjects were asked about and subjected to the preovulation period.

The study's methodology lasted for six weeks. In addition to the neurological rehabilitation program, the RRG group received robotic rehabilitation twice a week. Robotic rehabilitation was performed for 40 min per session. In addition to the neurological rehabilitation program, the VRRG group received non-invasive taVNS and robotic rehabilitation twice a week. For 20 min, a non-invasive auricular taVNS was used. The researcher conducted several assessments at two distinct points in time during the investigation. These intervals were scheduled and carried out both before and after the six-week treatment period. Given the relatively low number of stimulation sessions dictated by the robotic rehabilitation schedule, bilateral auricular stimulation was deliberately selected to augment afferent vagal input and enhance neuromodulatory efficacy within a feasible clinical protocol. Transcutaneous auricular vagus nerve stimulation was administered after each robotic rehabilitation session and was not delivered simultaneously with robotic training.

Vagus nerve stimulation

The VRRG group received a bilateral application of taVNS. taVNS was conducted using the Vagustim device (Vagustim) at a frequency of 10 Hz, in biphasic mode, with a modulation mode and a pulse width of 300 μs [20]. Twelve The current intensity adjustment was maintained at this setting while being modified based on the subject's detection threshold.

The taVNS treatment administered to the VRRG group utilized the Vagustim® device (Fig. 3), with bilateral stimulation applied to the tragus and concha regions of the ear via surface electrodes. Prior to each session, the electrodes were positioned on the skin surface using conductive gel by the same physiotherapist, following anatomical landmarks to ensure standardized application. Stimulation parameters were set at a frequency of 10 Hz, a pulse width of 300 μs, and a modulation mode wherein pulse width and frequency automatically varied by 50% within a 1-second cycle [21]. The stimulation duration was fixed at 20 min, based on prior evidence demonstrating

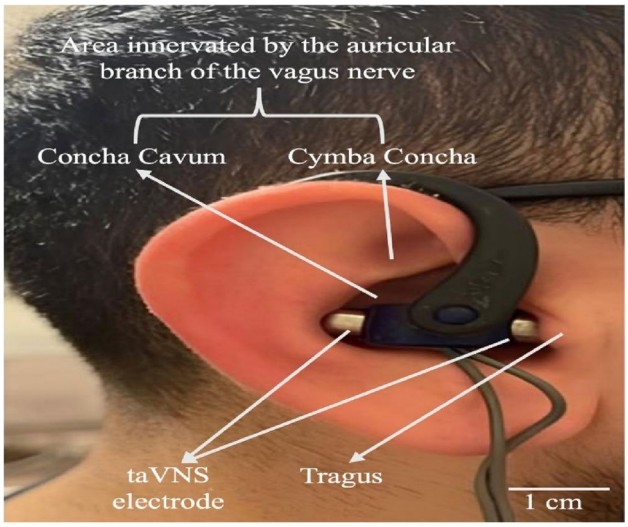

Fig. 3 Transcutaneous auricular vagus nerve stimulation (taVNS) electrode placement. Bilateral stimulation was delivered using the Vagustim® device with surface electrodes positioned on the tragus and concha (cymba/cavum) regions as shown. Stimulation was applied at 10 Hz with a 300 µs pulse width for 20 min, with intensity adjusted to a perceptible but comfortable level (modulation ± 50% within a 1-s cycle)

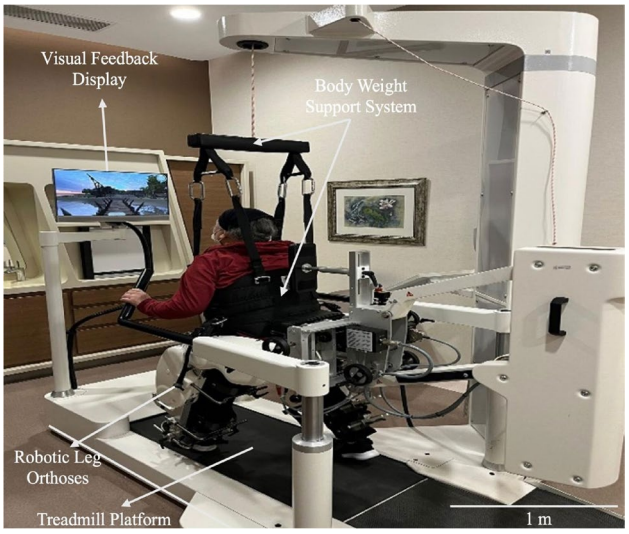

Fig. 4 Robotic gait training using the Lokomat (Hocoma) device (40 min/session, twice weekly for 6 weeks; 1.5 km/h)

therapeutic efficacy [22]. Current intensity was individually adjusted to a perceptible yet comfortable level for each participant and maintained consistently throughout the sessions, with tolerance thresholds reassessed before every application.

The stimulation parameters used in the present study were selected based on prior evidence from stroke-related transcutaneous auricular vagus nerve stimulation (taVNS) studies, with particular emphasis on safety, tolerability, and clinical feasibility. A stimulation frequency of 10 Hz has been previously applied in post-stroke populations and demonstrated clinical benefits while maintaining good tolerability, especially in studies targeting post-stroke dysphagia and motor recovery [18, 19]. Low-frequency stimulation (≤ 10 Hz) is considered appropriate for repeated application in stroke survivors, as it effectively engages vagal afferent pathways without excessive neural excitation.

A pulse width of 300 µs, combined with a modulation mode (± 50%), was selected to optimize afferent fiber recruitment and reduce habituation during stimulation sessions. The session duration of 20 min aligns with commonly reported taVNS protocols in stroke and neurological populations and represents a conservative yet therapeutically meaningful exposure [18, 22].

Regarding treatment dosage, taVNS was administered twice weekly for six weeks, resulting in a total of 12 sessions. Compared with studies employing daily or high-frequency stimulation schedules, the present protocol reflects a conservative dosing strategy, intentionally designed to complement robotic rehabilitation while minimizing participant burden. This approach allows evaluation of the additive effects of taVNS under clinically realistic rehabilitation conditions rather than maximal neuromodulatory exposure [19]. Although left-sided transcutaneous auricular vagus nerve stimulation is more commonly reported, previous evidence indicates that the laterality of taVNS (left, right, or bilateral) influences autonomic and neurophysiological responses, with bilateral stimulation engaging broader response patterns in experimental settings [23]. The taVNS schedule (twice weekly for six weeks; total of 12 sessions) was aligned with the robotic rehabilitation program to ensure clinical feasibility and participant adherence within a combined intervention design.

Robotic rehabilitation

Under the supervision of a physiotherapist who had received training from the Hocoma firm, Lokomat applications were carried out on the Lokomat Nanos model (Fig. 4). For six weeks, Lokomat was used twice a week for forty minutes each time. The Lokomat speed during walking training was set at 1.5 km/h [12]. By attaching the patient to the exoskeleton system, the pelvis was stabilized, and sufficient dorsiflexion, hip flexion, and knee flexion were guaranteed to place the affected extremity in full contact with the base. Additionally, sufficient heel striking was enabled to assure equitable weight transfers. The patient was made to sit properly, with no hip circumduction or pelvic elevation, to prevent compensating movements during training [24].

Gait training with the Lokomat device was structured based on key motor learning principles, specifically repetition, task specificity, and feedback. During each session, patients were guided using verbal instructions and

real-time visual feedback to achieve the targeted number of steps. Additionally, specific numerical goals were set to enhance intrinsic motivation.

Device calibration was manually performed by the therapist at the beginning of the training, tailored to each patient's anthropometric measurements. Alignment was ensured between the robotic axes and the anatomical axes of the hip, knee, and ankle joints. Parameters such as body weight support, guidance force, and step length were individually adjusted according to each participant's tolerance and were reassessed weekly. As indicated in the literature, these individualized adjustments not only promote safe mobilization but also provide sensorimotor input that supports neuroplasticity [10]. In this regard, the Lokomat device served not merely as a passive gait trainer but as a platform that actively facilitates motor learning. The robotic rehabilitation protocol was standardized across participants regardless of Brunnstrom stage. However, training parameters such as walking speed, body-weight support, and guidance force were individually adjusted according to each patient's functional capacity and tolerance.

Neurological rehabilitation

Each volunteer underwent a neurological rehabilitation program administered by skilled physiotherapists. Over the course of six weeks, the study's volunteer participants received neurological rehabilitation treatments five times a week for 30 min each [25].

In bed, the afflicted extremity received range of motion, massage, stretching, and strengthening exercises. Exercises included stepping in parallel bars, shifting weight to the side that was impacted, stair climbing and descending, walking forward, sideways, and backward, walking over obstacles, tandem walking, using a bicycle and hand ergometer, getting up from a sitting position to a standing one, and standing on a half-balance ball [26–29].

One of the electrotherapy techniques, neuromuscular electrical stimulation (NMES), was applied to the afflicted extremity for 20 min [30]. NMES was applied to the paretic lower limb muscles involved in gait performance. Specifically, NMES was delivered to the tibialis anterior and quadriceps femoris muscles using surface electrodes. Stimulation parameters were set as follows: biphasic symmetrical waveform, pulse frequency of 35 Hz, pulse duration of 300 μs, and an on–off cycle of 10 s on and 20 s off. Stimulation intensity was individually adjusted to elicit a visible and tolerable muscle contraction without causing discomfort. Each NMES session lasted 20 min and was performed under the supervision of a physiotherapist.

Table 1 Adherence and safety outcomes

Parameter	RRG	VRRG
Planned intervention duration	6 weeks	6 weeks
Number of robotic rehabilitation sessions	Identical	Identical
Standard neurological rehabilitation (content and duration)	Identical	Identical
NMES (as part of the standard program)	Yes	Yes
taVNS application	No	Yes
Number of taVNS sessions	-	12
Session attendance rate (%)	100%	100%
Temporary discontinuations	0	0
Dropouts	0	0
Adverse events	None	None

Sample size

The sample size was calculated for a 2 × 2 mixed design, including one between-subject factor (two levels) and one within-subject repeated-measures factor (two levels). The power analysis was conducted assuming a large effect size (f = 0.50), with a Type I error rate of $\alpha = 0.05$ and a Type II error rate of $\beta = 0.20$ (statistical power = 80%) [31], indicating that a minimum of 18 participants per group was required. Considering a potential 10% loss to follow-up, the sample size was increased to ensure adequate statistical power to detect differences between intervention procedures and to compensate for possible missing data during follow-up; accordingly, 20 participants per group, for a total of 40 participants, were included in the study. Sample size estimation was performed using G*Power software (version 3.1.9.7) by activating the "as in SPSS" option in the Options menu. It should be noted that an effect size of f = 0.50 represents a large effect rather than a medium one.

Randomization

Participants were randomly allocated to either the Robotic Rehabilitation Group (RRG) or the Vagus and Robotic Rehabilitation Group (VRRG) in a 1:1 ratio using a computer-generated block randomization procedure with a fixed block size of four. The randomization sequence was generated using IBM SPSS Statistics version 26.0 by an independent researcher who was not involved in participant recruitment, intervention delivery, or outcome assessment, thereby minimizing allocation bias. Stratified or matched randomization was not employed. Instead, baseline demographic and clinical characteristics—including age, sex, affected side, body mass index, and time since stroke—were evaluated after randomization to assess group comparability. As shown in Table 1, no statistically significant differences were observed between groups, indicating adequate baseline homogeneity despite the relatively small sample size. Allocation concealment was ensured using sequentially numbered, opaque, sealed envelopes, which were securely stored and opened sequentially only after

participant enrollment and the provision of written informed consent.

Blinding

Participant blinding was not feasible, as participants could recognize key aspects of the interventions they received. However, to minimize observer bias, the assessor responsible for outcome measurements and the specialist physician conducting the EMG analyses were blinded to group allocation. Throughout the evaluation process, group assignments were withheld, and all data were coded to maintain blinding integrity. During data processing and statistical analysis, datasets were anonymized and labeled using neutral group codes, and the researcher performing the statistical analyses was not informed of the actual group identities until all analyses were completed.

Outcome measures

The primary outcome measures of this randomized clinical trial were walking speed (10-Meter Walk Test), lower extremity motor function assessed by the Fugl–Meyer Assessment, and pain intensity measured using the Numerical Pain Rating Scale. These outcomes were selected a priori based on their clinical relevance to functional recovery after ischemic stroke and were predefined as confirmatory endpoints.

Secondary outcome measures included electrophysiological parameters (H-reflex and F-wave measurements) and stroke-specific quality of life. These secondary outcomes were predefined to provide exploratory and supportive information regarding potential neurophysiological mechanisms and broader patient-reported outcomes associated with the interventions.

Numerical pain rating scale

A sensitive measurement of pain is provided by the numerical pain rating scale. It is a subjective representation of the patient's present level of pain. With numbers ranging from 0 to 10, it is a simpler scale for the majority of people to comprehend [32].

Stroke specific quality of life scale

The stroke-specific quality of life scale is one of the most thorough measures of stroke patients' quality of life and is frequently used in both clinical settings and research [33]. There are 12 domains and 49 items in the stroke-specific quality of life measure. The score for each question ranges from 1 (strongly agree) to 5 (strongly disagree). The overall score ranges from 49 to 245 points. The lowest quality of life is represented by a score of 49, while the highest quality of life is represented by a score of 245 [34].

10 meter walk test

A popular clinical tool for evaluating walking speed in stroke therapy is the 10-meter walk test (10MWT). This test, which is easy to perform, measures how long it takes a patient to walk 10 m at their maximal speed or preferred pace. It is frequently used to assess gait speed as a crucial sign of functional mobility and stroke patients' progress toward recovery. Increases in gait speed as determined by the 10MWT are linked to improved recovery outcomes overall, such as increased mobility and independence in everyday activities [35].

Fugl-Meyer assessment scale

Reflexes, flexor and extensor synergies, and isolated movements are all measured on this scale to evaluate lower extremity motor function following a stroke. Higher scores indicate better function; the average total score is 34 points [36].

Electromyography

Biomedical tools called electromyography (EMG) devices are used to measure and examine the electrical activity of muscles. These gadgets identify and graphically represent the electrical impulses that muscles produce in response to brain stimulation. EMG equipment is essential for evaluating muscle function and identifying neurological conditions. They are frequently used in rehabilitation to track and assess how well a patient is responding to treatment, especially in diseases like stroke that cause loss of motor function [37].

Before and six weeks following the commencement of treatment, a neurologist used the Synergy software to perform surface EMG on the affected side and electrophysiological exams using an EMG equipment (Natus UltraPro S100). A five-year-experienced neurologist conducted the measurements. The patient was laying on the examination stretcher in supine and prone positions, with their eyes closed but alert, in a quiet room with a temperature between 24 °C and 25 °C. The area was cleansed with alcohol, and the electrodes were positioned parallel to the muscle fibers. To avoid signal loss during the measurement, cell phones were not permitted in the room. Caffeine and tobacco use were discouraged for at least eight hours before to the electrophysiologic examination. We told them before the measurement that their legs should be trimmed if they had hair growth on them.

With the individual lying prone on the examination table and their ankles in the neutral position (90°), superficial electrodes were placed across the gastrocnemius muscle to perform H-reflex measurements. To assess the H-reflex and M response, the reference electrode was positioned around 4 cm distal to the active electrode, which was positioned in the center of the poplitea and medial malleolus. 60 msec was the sweep rate, 500

μV was the sensitivity, 0.5 Hz was the frequency, and 1 msec was the stimulation time. The evaluation form included the mean latencies, Mmax amplitudes, and Hmax amplitudes of the H-reflex parameters that were acquired as output following the measurement. The lower extremity's afflicted side was used for measurements. Electromyographic outcomes were analyzed using within-muscle normalization approaches, such as the Hmax/Mmax ratio, which are widely accepted to account for inter-individual variability in muscle mass, electrode placement, and peripheral conduction properties. Therefore, additional normalization using contralateral (unaffected) muscle measurements was not applied.

Due to the nature of the intervention, participant blinding was not feasible; however, to mitigate measurement bias, the specialist physician conducting the EMG analyses and the researchers responsible for outcome evaluations remained blinded to group allocation. All EMG data were coded during transmission, further minimizing observer bias throughout the assessment process. Moreover, electrode placement and current intensity were standardized in strict accordance with the protocol, thereby enhancing methodological rigor and reproducibility.

The H-reflex assessment was limited to the gastrocnemius muscle, as it is widely regarded as a reliable indicator of segmental spinal reflex excitability in post-stroke populations. The gastrocnemius H-reflex is frequently used in clinical and experimental studies due to its reproducibility, clear neurophysiological interpretability, and clinical relevance to gait-related motor control [38, 39]. Assessment of additional lower-limb muscles was not performed in order to reduce participant burden and to maintain methodological consistency. Given the clinical characteristics of the study population and the comprehensive intervention protocol, the inclusion of multiple muscle-specific H-reflex measurements was not prioritized, as the primary aim was to evaluate global changes in spinal reflex modulation rather than muscle-specific excitability patterns.

Adherence and safety

All participants completed the intervention period, and no dropouts occurred in either group. Session attendance was monitored throughout the study, and all participants attended all scheduled sessions, resulting in a 100% adherence rate. No temporary discontinuations or missed sessions were recorded during the intervention period.

Both groups received identical content and duration of the standard neurological rehabilitation program, including neuromuscular electrical stimulation (NMES) and robotic rehabilitation, in accordance with the study protocol. Transcutaneous auricular vagus nerve stimulation (taVNS) was applied only in the VRRG as an additional intervention. No adverse events or intervention-related complications were observed in either group during or after the intervention period. Adherence to the intervention protocol and safety outcomes, including session attendance, temporary discontinuations, and adverse events, are summarized in Table 1.

Statistical analysis

The normality of continuous variables was assessed both graphically and analytically using the Shapiro–Wilk test. Descriptive statistics were presented as mean ± standard deviation for continuous variables and as number (n) and percentage (%) for categorical variables. Group differences in categorical variables (gender, dominant side, and affected side) were examined using the chi-square (χ^2) test or Fisher's exact test, as appropriate. For between-group comparisons at baseline and post-treatment, the Independent Samples t-test was used for normally distributed variables, whereas the Mann–Whitney U test was applied for non-normally distributed variables. Within-group pre–post comparisons were conducted using the Paired Samples t-test for normally distributed variables and the Wilcoxon Signed-Rank test for non-normally distributed variables. To assess whether changes over time (pre-treatment vs. post-treatment) differed between the two intervention groups (RRG and VRRG), a two-way mixed analysis of variance (group × time interaction) was performed. When the assumptions of parametric analysis were not met, longitudinal data were analyzed using the nonparametric F1-LD-F1 design implemented in the nparLD package in R, which is specifically developed for factorial longitudinal data with repeated measurements.

Effect sizes (r) were calculated to quantify the magnitude of both within-group and between-group effects and were interpreted as small (0.10–0.29), medium (0.30–0.49), or large (≥ 0.50). In addition to p-values, mean differences and 95% confidence intervals (CI) were reported to facilitate clinical interpretation of the findings. Given the number of outcome measures assessed, no formal correction for multiple comparisons was applied. This decision was based on the prespecification of primary outcomes—walking speed, motor function, and pain intensity—as confirmatory endpoints. Analyses of secondary outcomes, including electrophysiological parameters and quality-of-life measures, were conducted for exploratory purposes; therefore, corresponding p-values should be interpreted cautiously, with greater emphasis placed on effect sizes, confidence intervals, and consistency of results across outcomes. All statistical analyses were performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Nonparametric longitudinal analyses were conducted using the R statistical

environment (RStudio) with the nparLD package. Statistical significance was set at $p < 0.05$.

Results

Accordingly, results related to primary outcome measures are presented first, followed by secondary outcome measures, which are reported for exploratory purposes.

No statistically significant differences were observed in the demographic characteristics of the participants between the groups ($p > 0.05$) (Table 2).

No statistically significant difference was observed between the groups in pre-treatment Hmax/Mmax amplitude (unaffected side) values ($p > 0.05$). However, a statistically significant difference was detected between the groups in the post-treatment measurements ($z = 1.966$, $p = 0.049$), indicating that the mean post-treatment Hmax/Mmax amplitude (unaffected side) was higher in the RRG group compared with the VRRG group. Apart from this finding, no statistically significant differences were found between the groups in pre- and post-treatment comparisons for the 10 m Walk Test, Fugl–Meyer Assessment, H-reflex and F-tibial parameters, pain score, and stroke-specific quality of life ($p > 0.05$).

Within the RRG group, statistically significant time-dependent changes were observed between pre-treatment and post-treatment measurements in the 10 m Walk Test, Fugl–Meyer Assessment, H-reflex and F-tibial parameters, and stroke-specific quality of life ($p < 0.05$). Post-treatment measurements demonstrated an increase in Fugl–Meyer Assessment and stroke-specific quality of life scores, whereas a reduction was observed in 10 m Walk Test duration and in the majority of H-reflex and F-tibial parameters.

Within the VRRG group, statistically significant time-dependent changes were also identified between pre-treatment and post-treatment measurements in the 10 m Walk Test, Fugl–Meyer Assessment, H-reflex and F-tibial parameters, pain score, and stroke-specific quality of life ($p < 0.05$). Following treatment, Fugl–Meyer Assessment and stroke-specific quality of life scores increased, while 10 m Walk Test duration, H-reflex and F-tibial parameters, and pain scores decreased.

In the mixed-model analysis, the time × treatment interaction was found to be statistically significant for the 10 m Walk Test, F-tibial mean latency (affected side), F-tibial mean amplitude (affected side), and pain score (group × time interaction, $p < 0.05$), indicating that the effects of the treatments differed over time. Moreover, VRRG treatment resulted in a greater reduction in these parameters compared with RRG treatment (Table 3).

The greater reduction in the Hmax/Mmax amplitude ratio observed in the RRG indicates a more pronounced modulation of segmental spinal reflex excitability in this group, whereas the VRRG demonstrated superior functional improvements in walking speed and pain intensity. When the difference analysis was compared according to the groups, statistically significant differences were found in 10-meter walking test ($p = 0.006$), H Max/M Max Amplitude / Affected Side ($p = 0.032$), F Tibial Mean Latency / Affected Side (ˆ0.001), F tibial mean amplitude / Affected Side ($p = 0.002$), F tibial mean latency / Unaffected Side ($p = 0.005$), Pain Scale Score ($p = 0.048$) (Table 4).

Table 2 Comparison of demographic characteristics between groups

		RRG ($n = 20$)	VRRG ($n = 20$)	t; χ^2	p
Age (years)	Mean ± SD	54.45 ± 7.70	55.10 ± 5.74	t = 0.303	0.764
	Median (Min-Max)	55.5 (40–65)	56.0 (42–65)		
BMI (kg/m^2)	Mean ± SD	26.33 ± 2.97	25.86 ± 1.79	t = 0.607	0.547
	Median (Min-Max)	26.1 (20.0-31.2)	25.7 (22.2–29.1)		
Gender, n (%)					
Female		11 (55.0)	9 (45.0)	$\chi 2$ =0.400	0.527
Male		9 (45.0)	11 (55.0)		
Dominant Side, n (%)					
Right		15 (75.0)	17 (85.0)	-	0.347*
Left		5 (25.0)	3 (15.0)		
Affected Side, n (%)					
Right		10 (50.0)	10 (50.0)	$\chi 2$ =0.001	0.999
Left		10 (50.0)	10 (50.0)		

SD Standard Deviation, *RRG* Robotic Rehabilitation Group, *VRRG* Vagus and Robotic Rehabilitation Group

Normality was assessed using the Shapiro–Wilk test (α = 0.05). Age and BMI met normality and were compared using the Independent Samples t-test (t). Categorical variables were compared using the Chi-square test (χ^2) or Fisher's exact test (*) when appropriate

Discussion

In the present study, both robotic rehabilitation alone and combined taVNS with robotic rehabilitation resulted in significant improvements in functional outcomes. The combined intervention was associated with greater improvements in walking speed and pain, whereas robotic rehabilitation alone showed a greater reduction in the Hmax/Mmax amplitude ratio. No consistent between-group differences were observed for the remaining electrophysiological parameters.

Importantly, the observed between-group improvement in the 10-Meter Walk Test (10MWT) exceeded commonly reported minimal clinically important difference (MCID) values for post-stroke gait speed (approximately 0.10–0.16 m/s), indicating that the observed changes were not only statistically significant but also clinically meaningful [40, 41]. Similarly, improvements in lower extremity motor function, as assessed by the Fugl–Meyer Assessment–Lower Extremity (FMA-LE),

Table 3 Within-group and between-group comparison of parameters

Parameters	RRG (*n* = 20)		VRRG (*n* = 20)		*p*(Group)		GTI
	Mean ± SD	Median (Min-Max)	Mean ± SD	Median (Min-Max)			
10mt Walking Test (sn)							
Pre-Treatment	26.95 ± 8.48	26.1 (15.9–50.2)	29.35 ± 5.53	28.9 (20.1–38.7)	t = 1.059	0.296	**0.014**
Post Treatment	24.25 ± 7.19	23.3 (14.0-45.8)	24.81 ± 4.64	24.9 (18.1–34.5)	t = 0.289	0.774	
p(Time)	*t = 5.273; p < **0.001**		*t = 9.056; p < **0.001**				
r	0.771		0.901				
Mean Difference (%95 CI)	-2.70 (-3.76; -1.62)		-4.54 (-5.59; -3.49)				
Fugl Meyer Score							
Pre-Treatment	16.75 ± 3.46	17.0 (9–23)	16.30 ± 3.28	17.0 (10–23)	t = 0.422	0.675	0.090
Post Treatment	21.40 ± 3.28	21.0 (17–28)	22.60 ± 3.66	22.0 (17–28)	t = 1.091	0.282	
p(Time)	*t = 7.154; p < **0.001**		*t = 9.149; p < **0.001**				
r	0.854		0.903				
Mean Difference (%95 CI)	4.65 (3.29; 6.01)		6.30 (4.86; 7.74)				
H Mean Latency – Affected Side							
Pre-Treatment	30.95 ± 1.13	30.6 (29.0-33.9)	31.14 ± 1.14	31.2 (28.5–32.7)	t = 0.534	0.596	0.638
Post- Treatment	30.64 ± 1.08	30.3 (28.9–33.1)	30.88 ± 1.06	31.0 (28.3–32.5)	t = 0.719	0.476	
p(Time)	*t = 3.802; p = **0.001**		*t = 3.723; p = **0.001**				
r	0.657		0.649				
Mean Difference (%95 CI)	-0.31 (-0.48; -0.14)		-0.26 (-0.41; -0.11)				
Hmax/Mmax Amplitude – Affected Side							
Pre-Treatment	0.39 ± 0.09	0.41 (0.17–0.50)	0.36 ± 0.06	0.36 (0.27–0.46)	z = 1.721	0.086	0.060
Post Treatment	0.36 ± 0.08	0.38 (0.16–0.46)	0.35 ± 0.06	0.35 (0.26–0.46)	z = 1.003	0.327	
p(Time)	*z = 3.235; p = **0.001**		*z = 2.582; p = **0.010**				
r	0.596		0.509				
Mean Difference (%95 CI)	-0.03 (-0.04; -0.01)		-0.01 (-0.02; -0.002)				
H Mean Latency – Unaffected Side							
Pre-Treatment	30.35 ± 1.16	30.1 (29.0-33.1)	30.68 ± 1.26	30.9 (28.0-32.2)	t = 0.878	0.385	0.955
Post Treatment	30.36 ± 1.18	30.1 (29.0-33.1)	30.69 ± 1.26	30.9 (28.0-32.2)	t = 0.867	0.391	
p(Time)	*t = 0.609; *p* = 0.550		*t = 0.375; *p* = 0.711				
r	0.138		0.086				
Mean Difference (%95 CI)	0.01 (-0.02; 0.04)		0.01 (-0.04; 0.05)				
Hmax/Mmax Amplitude – Unaffected Side							
Pre-Treatment	0.38 ± 0.09	0.42 (0.17–0.50)	0.35 ± 0.05	0.35 (0.26–0.44)	z = 1.954	0.052	0.134
Post Treatment	0.38 ± 0.08	0.40 (0.17–0.49)	0.35 ± 0.06	0.35 (0.26–0.44)	z = 1.966	**0.049**	
p(Time)	*z = 2.516; p = **0.012**		*z = 0.686; *p* = 0.493				
r	0.4999		0.155				
Mean Difference (%95 CI)	-0.006 (-0.01; -0.001)		-0.002 (-0.005; 0.001)				
F Tibial Mean Latency – Affected Side							
Pre-Treatment	49.43 ± 4.33	49.4 (42.0-59.2)	48.94 ± 4.69	49.6 (40.0-56.4)	t = 0.343	0.733	**0.002**
Post Treatment	49.12 ± 4.27	48.9 (42.0-59.1)	48.00 ± 4.44	48.8 (39.8–56.1)	t = 0.812	0.422	
p(Time)	*t = 2.784; p = **0.012**		*t = 5.901; p < **0.001**				
r	0.538		0.804				
Mean Difference (%95 CI)	-0.31 (-0.54; -0.08)		-0.94 (-1.27; -0.60)				
F Tibial Mean Amplitude – Affected Side							
Pre-Treatment	307.34 ± 37.02	315.9 (250.5-360.4)	319.60 ± 37.28	325.1 (260.4-370.8)	t = 1.044	0.303	**0.001**
Post Treatment	301.09 ± 35.84	315.4 (240.9-350.1)	304.00 ± 33.70	307.9 (245.8-360.8)	t = 0.264	0.793	
p(Time)	*t = 5.180; p < **0.001**		*t = 7.035; p < **0.001**				
r	0.765		0.850				
Mean Difference (%95 CI)	-6.25 (-8.77; -3.72)		-15.60 (-20.25; -10.96)				
F Tibial Mean Latency – Unaffected Side							
Pre-Treatment	48.81 ± 4.36	49.1 (41.0-58.9)	47.70 ± 4.54	48.6 (39.8–55.4)	t = 0.786	0.437	0.156
Post Treatment	48.63 ± 4.31	48.2 (41.0-58.8)	47.24 ± 4.38	48.5 (39.5–54.9)	t = 1.011	0.319	

Table 3 (continued)

Parameters	RRG (*n* = 20)		VRRG (*n* = 20)		*p*(Group)		GTI
	Mean ± SD	Median (Min-Max)	Mean ± SD	Median (Min-Max)			
p(Time)	*t = 1.124; *p* = 0.275		*t = 4.453; p < **0.001**				
r	0.249		0.715				
Mean Difference (%95 CI)	-0.18 (-0.53; 0.16)		-0.46 (-0.68; -0.25)				
F Tibial Mean Amplitude – Unaffected Side							
Pre-Treatment	299.25 ± 35.61	310.8 (245.9-350.1)	302.31 ± 34.83	297.8 (250.5-383.6)	t = 0.275	0.785	0.248
Post Treatment	293.97 ± 33.13	303.7 (245.9-341.1)	299.94 ± 36.07	295.0 (245.6-380.9)	t = 0.546	0.589	
p(Time)	*t = 2.457; p = **0.024**		*t = 1.902; *p* = 0.072				
r	0.491		0.399				
Mean Difference (%95 CI)	-5.28 (-9.78; -0.78)		-2.37 (-4.96; 0.24)				
F Tibial Persistence – Affected Side							
Pre-Treatment	70.84 ± 7.89	73.2 (57.0-82.1)	72.91 ± 8.52	74.1 (59.4–84.6)	t = 0.797	0.430	0.098
Post Treatment	68.82 ± 8.26	72.5 (55.0-79.9)	69.37 ± 7.69	70.4 (56.1–82.3)	t = 0.218	0.829	
p(Time)	*t = 4.306; p < **0.001**		*t = 4.630; p < **0.001**				
r	0.703		0.728				
Mean Difference (%95 CI)	-2.02 (-3.00; -1.04)		-3.54 (-5.14; -1.94)				
F Tibial Persistence – Unaffected Side							
Pre-Treatment	68.59 ± 8.63	70.9 (56.1–84.0)	68.96 ± 7.96	67.9 (57.1–87.5)	t = 0.141	0.889	0.253
Post Treatment	67.41 ± 7.79	70,4 (56.1–77.8)	68.41 ± 8.23	67.3 (56.0-86.9)	t = 0.397	0.694	
p(Time)	*t = 2.537; p = **0.020**		*t = 1.926; *p* = 0.069				
r	0.503		0.404				
Mean Difference (%95 CI)	-1.18 (-2.16; -0.21)		-0.55 (-1.15; 0.05)				
Pain Scale Score							
Pre-Treatment	3.20 ± 2.80	4.0 (0–8)	3.40 ± 2.76	3.0 (0–9)	z = 0.235	0.820	**0.044**
Post Treatment	2.90 ± 2.38	3.0 (0–7)	1.55 ± 2.23	0.0 (0–5)	z = 1.759	0.102	
p(Time)	*z = 0.637; *p* = 0.524		*z = 2.878; p = **0.004**				
r	0.145		0.551				
Mean Difference (%95 CI)	-0.30 (-1.48; 0.88)		-1.85 (-2.87; -0.83)				
Stroke-Specific Quality of Life							
Pre-Treatment	147.20 ± 30.62	147.0 (85–191)	142.60 ± 22.92	144.0 (111–207)	t = 0.538	0.594	0.058
Post Treatment	156.05 ± 33.78	164.0 (89–215)	161.70 ± 23.45	162.0 (122–216)	t = 0.614	0.543	
p(Time)	*t = 3.577; p = **0.002**		*t = 4.141; p = **0.001**				
r	0.634		0.688				
Mean Difference (%95 CI)	8.85 (3.67; 14.03)		19.10 (9.45; 28.75)				

RRG Robotic Rehabilitation Group, *VRRG* Vagus and Robotic Rehabilitation Group, *SD* Standard Deviation, *CI* Confidence Interval, *GTI* Group × Time Interaction

Normality was assessed with the Shapiro–Wilk test (α = 0.05). Normally distributed outcomes were analyzed with paired/independent t-tests and reported as t(df); non-normal outcomes were analyzed with Wilcoxon signed-rank/Mann–Whitney U and reported as z

t: Independent Samples t-test; *t: Paired Samples t-test; z: Mann–Whitney U test (reported as z); *z: Wilcoxon Signed-Rank test; r: effect size for nonparametric tests (r = Z/√N)

Highlighted (bold) *p*-values indicate statistical significance ($p < 0.05$)

approached or exceeded published MCID thresholds (approximately 4–6 points), supporting the functional relevance of the observed motor gains [42].

The differential effects observed between groups may be explained by distinct neurophysiological mechanisms. Robotic gait training primarily provides repetitive, task-specific sensorimotor input that may influence spinal and subcortical circuits, whereas taVNS is thought to exert its effects predominantly at supraspinal levels by modulating cortical excitability and facilitating motor learning. Accordingly, the addition of taVNS may preferentially enhance functional gait-related outcomes, such as walking speed, without necessarily inducing parallel changes in segmental spinal reflex excitability.

Improvements observed in walking speed, motor function, and pain represent confirmatory findings of this trial, whereas changes in electrophysiological parameters and quality of life should be interpreted as exploratory outcomes that provide supportive mechanistic insights rather than definitive efficacy evidence.

An important and counter-intuitive finding of the present study was the greater reduction in the Hmax/Mmax

Table 4 Comparison of post-treatment and pre-treatment differences by groups

Parameters	RRG Mean ± SD (Median)	VRRG Mean ± SD (Median)	Mann-Whitney	*r*	*P*	95% CI (Median Difference, VRRG–RRG)
10mt Walking Test	-2.70 ± 2.29 (-2.1)	-4.54 ± 2.24 (-4.4)	99.0	0.432	**0.006**	-3.7 to -0.7
Fugl Meyer Score	4.65 ± 2.91 (5.0)	6.30 ± 3.08 (5.5)	144	0.240	0.127	-0.5 to 2.5
H Mean Latency / Affected Side	-0.31 ± 0.37 (-0.1)	-0.26 ± 0.31 (-0.2)	188.0	0.051	0.745	-0.15 to 0.25
H Max/M Max Amplitude / Affected Side	-0.03 ± 0.03 (0.0)	-0.01 ± 0.02 (0.0)	122.0	0.334	**0.032**	0.00 to 0.03
H Mean Latency / Unaffected Side	0.01 ± 0.07 (0.0)	0.01 ± 0.10 (0.0)	175.0	0.107	0.484	-0.04 to 0.06
H Max/M Max Amplitude / Healthy Side	-0.01 ± 0.01 (0.0)	0.00 ± 0.01 (0.0)	146.0	0.231	0.111	-0.01 to 0.02
F Tibial Mean Latency / Affected Side	-0.31 ± 0.50 (-0.1)	-0.94 ± 0.71 (-0.8)	61.0	0.595	**<0.001**	-1.2 to -0.3
F tibial mean amplitude / Affected Side	-6.25 ± 5.40 (-5.0)	-15.61 ± 9.92 (-15.2)	83.0	0.500	**0.002**	-14.2 to -4.0
F tibial persistence / Affected Side	-2.02 ± 2.10 (-1.4)	-3.54 ± 3.42 (-3.4)	139.5	0.259	0.056	-2.9 to 0.0
F tibial mean latency / Unaffected Side	-0.18 ± 0.74 (0.0)	-0.47 ± 0.47 (-0.3)	95.5	0.447	**0.005**	-0.6 to -0.1
F tibial mean amplitude / Unaffected Side	-5.28 ± 9.61 (-4.6)	-2.36 ± 5.56 (-0.9)	148.5	0.220	0.163	-1.0 to 5.8
F tibial persistence / Unaffected Side	-1.19 ± 2.09 (-1.1)	-0.55 ± 1.28 (-0.2)	145.5	0.233	0.139	-0.3 to 1.7
Pain Scale Score	-0.30 ± 2.52 (0.0)	-1.85 ± 2.18 (-1.5)	129.0	0.304	**0.048**	-2.5 to -0.1
Stroke-Specific Quality of Life Score	8.85 ± 11.07 (7.5)	19.10 ± 20.63 (15.0)	139.5	0.259	0.101	-1.8 to 17.2

SD Standard Deviation, *RRG* Robotic Rehabilitation Group, *VRRG* Vagus and Robotic Rehabilitation Group, *r* Effect size

Bold *p*-values indicate statistical significance ($p < 0.05$)

amplitude ratio in the RRG compared with the VRRG. The H-reflex and Hmax/Mmax ratio are commonly interpreted as indicators of segmental spinal reflex excitability rather than direct measures of supraspinal motor control. Robotic gait training may preferentially modulate spinal inhibitory circuits through repetitive, task-specific proprioceptive input, whereas taVNS primarily influences supraspinal networks involved in gait performance and pain modulation. Accordingly, electrophysiological findings were interpreted as exploratory and complementary to the observed functional outcomes and evaluated alongside effect sizes and confidence intervals.

Prior taVNS studies have reported beneficial effects on post-stroke recovery when paired with rehabilitation [18, 19]; however, evidence regarding gait-related outcomes and its combination with robot-assisted locomotor training remains limited.

Previous research has consistently demonstrated that robot-assisted gait training improves motor function, walking performance, and functional outcomes in individuals with stroke and other neurological conditions [43, 44]. Consistent with this literature, the robotic rehabilitation group in the present study showed significant improvements in motor function, walking speed, and quality of life. Changes observed in H-reflex parameters may provide insight into the neurophysiological mechanisms underlying these functional improvements. Reductions in H-reflex amplitude and latency are commonly interpreted as reflecting decreased spinal motoneuron pool excitability and enhanced presynaptic inhibition of Ia afferents [39, 45]. From a functional perspective, such modulation of spinal excitability may facilitate improved motor coordination during gait and contribute to increased walking speed. In parallel, reduced spinal hyperexcitability may attenuate nociceptive processing, providing a plausible neurophysiological link to the observed reductions in pain. These electrophysiological findings should be interpreted as exploratory and supportive of the clinical outcomes rather than as definitive efficacy markers.

Li et al. reported that stroke patients receiving taVNS in addition to conventional rehabilitation demonstrated greater improvements in lower extremity motor function compared with sham stimulation [19]. These findings are consistent with the present results and support the potential additive value of taVNS when combined with rehabilitation interventions.

One of the major strengths of this study is its innovative approach, which investigates the combined effects of robotic rehabilitation and taVNS. The randomized controlled clinical design allowed for a reliable comparison between interventions and enhanced the methodological validity of the findings. Furthermore, the inclusion of both clinical outcome measures (Fugl-Meyer Assessment, 10-Meter Walk Test, Pain Scale) and electrophysiological parameters (H-reflex and F-wave) enabled a comprehensive evaluation of outcomes at both functional and neurophysiological levels. The meticulous standardization of the intervention protocols in accordance with established literature further strengthened the consistency, reproducibility, and scientific rigor of the methodology.

The present study has several methodological limitations that should be considered when interpreting the findings. Due to the inherent nature of the interventions, participant and therapist blinding was not feasible, which

may have introduced expectation-related and performance-related bias, particularly for subjective or performance-based outcomes such as pain intensity, walking speed, and quality of life. To mitigate these potential sources of bias, both groups received identical rehabilitation content and session durations, standardized verbal instructions were applied, and all interventions were delivered by experienced physiotherapists in accordance with a predefined protocol. Outcome assessments were conducted by blinded assessors; however, expectancy effects cannot be entirely excluded.

Another limitation is the imbalance in total intervention time between groups, as the VRRG received additional taVNS sessions. Consequently, between-group differences cannot be attributed exclusively to taVNS and may partly reflect increased treatment exposure. In addition, the absence of a sham-taVNS control group limits the ability to isolate taVNS-specific effects, and future studies should incorporate sham conditions with matched intervention duration.

Electrophysiological assessment was limited to the gastrocnemius muscle, and EMG data were not normalized to contralateral muscle activity, which may affect the interpretation of neurophysiological findings. Furthermore, this single-center study design and the lack of systematic assessment of psychosocial factors may limit the generalizability of the results. Finally, the sample size calculation was based on a large assumed effect size ($f = 0.50$), which may have limited the detection of small-to-moderate between-group effects. Accordingly, non-significant findings should be interpreted cautiously.

Despite these limitations, the combined application of robotic rehabilitation and taVNS appears to be a promising approach for enhancing post-stroke motor recovery. Future multicenter studies with larger sample sizes, long-term follow-up, improved blinding strategies, and comprehensive neurophysiological and psychosocial assessments are warranted. Overall, the present findings should be interpreted as preliminary evidence supporting feasibility and potential efficacy rather than definitive proof of taVNS-specific effects.

Conclusion

In patients with ischemic stroke, adding taVNS to robotic rehabilitation resulted in greater improvements in walking speed and pain compared with robotic rehabilitation alone. No consistent between-group differences were observed for most electrophysiological outcomes, although robotic rehabilitation was associated with a greater reduction in the Hmax/Mmax amplitude ratio. No adverse events were reported.These findings suggest that robotic rehabilitation and taVNS may differentially influence functional and neurophysiological recovery, potentially through distinct mechanisms. Further sham-controlled studies are warranted to clarify the specific contribution of taVNS and to confirm these preliminary findings.

Abbreviations

taVNS	Transcutaneous Auricular Vagus Nerve Stimulation
VNS	Vagus Nerve Stimulation
WHO	World Health Organization
VRRG	Vagus and Robotic Rehabilitation Group
RRG	Robotic Rehabilitation Group
SD	Standard Deviation
EMG	Electromyography
10MWT	10-Meter Walking Test

Supplementary Information

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Supplementary Material 1.

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We thank all our subjects who voluntarily participated in our study.

Patient consent statement

An introduction to the survey stated that the information was kept confidential, that the results of the survey was anonymous, and that the responses could not be traced back to them. They consented to the survey by answering the questions.

Authors' contributions

Ö.D.K. and İ.H.U. were responsible for funding acquisition. Ö.D.K., İ.H.U., S.H.H., and A.V.Ö. contributed to the writing of the original draft. Conceptualization was performed by Ö.D.K., İ.H.U., S.H.H., and E.B.A. Methodology was designed by Ö.D.K., İ.H.U., and S.H.H. Investigation was conducted by Ö.D.K. and İ.H.U. Formal analysis, visualization, and data curation were carried out by Ö.D.K. Supervision was provided by İ.H.U., S.H.H., A.V.Ö., and E.B.A. Project administration was managed by İ.H.U., A.V.Ö., and E.B.A. S.H.H. and A.V.Ö. contributed to writing – review and editing, and validation was performed by S.H.H., A.V.Ö., and E.B.A. All authors read and approved the final manuscript.

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Data availability

The data that support the findings of this investigation are accessible upon request from the corresponding author.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Gümüşhane University Scientific Research and Publication Ethics Committee (approval date: 26 October 2022; approval no.: 2022/6). Written informed consent to participate was obtained from all participants prior to enrollment.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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