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# Comparison of Two Ultrasound-Guided Percutaneous Neuromodulation Protocols Applied to the Median Nerve on Maximal Handgrip Strength in Healthy Adults: A Randomized Clinical Trial

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## ABSTRACT

**Background:** Ultrasound (US)-guided percutaneous neuromodulation (PNM) has shown promising effects in the neuromuscular field, although its effects in healthy individuals remain unclear.

**Objective:** This study aimed to compare the immediate effects of two different US-guided PNM protocols applied to the median nerve on maximal handgrip strength and pain intensity during intervention in healthy adults.

**Materials and Methods:** A randomized clinical trial was conducted with evaluator and participant blinding, in which 86 healthy adults were assigned to two groups: protocol 1 (10 Hz, 250 μs, 10 seconds of stimulation followed by 10 seconds of rest) and protocol 2 (100 Hz, 350 μs, 5 seconds of stimulation followed by 55 seconds of rest), each receiving one isolated US-guided PNM session of the median nerve at an individualized, nonpainful, and well-tolerated intensity sufficient to elicit a visible muscle contraction. Maximal handgrip strength was assessed before and after the intervention using dynamometry. Pain intensity during intervention was measured using the Numerical Pain Rating Scale.

**Results:** No statistically significant changes were observed in maximal handgrip strength within groups or between groups. Regarding pain perceived by the participants during the PNM intervention, there were no statistically significant differences between the two groups.

**Conclusions:** A single session of US-guided PNM did not produce immediate significant improvements in maximal handgrip strength in healthy adults. No significant differences were found between the protocols studied, or in pain perception between groups during the application of the technique, which was safe and well-tolerated.

**Clinical Trial Registration:** The Clinicaltrials.gov registration number for the study is NCT07098130.

**Keywords:** Handgrip, healthy adults, muscle strength, percutaneous neuromodulation, ultrasonography

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## INTRODUCTION

Ultrasound (US)-guided percutaneous neuromodulation (PNM) is an invasive physiotherapy technique increasingly used in the management of neuromusculoskeletal disorders, including peripheral neuropathic pain, myofascial pain syndrome, osteoarthritis, chronic neck and low back pain, plantar fasciitis, and anterior knee pain.[1–4] In addition to its therapeutic applications in symptomatic populations, PNM also has been explored for modulating neuromuscular function in athletic individuals who are asymptomatic, when the aim is to optimize motor performance rather than treat pathology.[5–14] It involves applying electrical stimulation to peripheral nerves or musculoskeletal structures using a solid, filiform needle inserted percutaneously under US guidance,[15] enhancing the safety and efficacy of the procedure. This technique induces sensory or motor responses for various therapeutic purposes.

The therapeutic use of electrical stimulation has evolved from general applications to specific approaches for neuromuscular and musculoskeletal dysfunctions. The growing interest in US-guided PNM is evidenced by an increasing number of studies that support its effectiveness in neuromuscular potentiation and pain management in recent years. Notably, improvements in quadriceps isometric strength have been observed after application to the femoral nerve,[16] and benefits in muscle performance have been reported in dancers and athletes.[5,8,9] Additional studies have reported positive effects on hamstring flexibility,[11] radial nerve function in cases of lateral epicondylitis,[17] and even clinical outcomes comparable to surgical intervention in carpal tunnel syndrome.[18]

The electrical current used in US-guided PNM is typically biphasic, compensated, and delivered at low frequencies, generally ranging from 1 to 10 Hz and 80 to 100 Hz, with pulse widths between 50 and 500 μs, depending on the intended physiologic response and therapeutic objectives.[1,6,7,15,19,20] The selection of these parameters directly influences efficacy, thereby enabling the technique to be adapted to each patient.

The stimulation protocols used in this study were selected on the basis of two well-described physiologic phenomena associated with short-term and transient modulation of force production. An intermittent low-frequency protocol (10 Hz) was chosen on the basis of the staircase (treppe) phenomenon, in which repetitive low-frequency stimulation produces a progressive increase in force output, classically attributed to peripheral facilitation mechanisms.[21,22] In contrast, a high-frequency burst protocol (100 Hz) was selected on the basis of its association with tetanic activation and posttetanic potentiation, a phenomenon linked to an acute enhancement of force after brief high-frequency stimulation.[22–24] Recent human evidence indicates that posttetanic potentiation reflects a transient improvement in neuromuscular efficiency during subsequent voluntary contractions, primarily attributed to increased myofibrillar calcium ion sensitivity secondary to phosphorylation of myosin regulatory light chains and enhanced excitation–contraction coupling.[25,26] Although these mechanisms have been primarily described in muscle or motor-unit–stimulation paradigms, they provide a physiologic framework commonly used to guide frequency-dependent peripheral nerve stimulation strategies, with shorter pulse durations used for repetitive low-frequency stimulation and longer pulses for brief high-frequency bursts to ensure effective neural recruitment.

Despite emerging evidence supporting frequency-dependent neuromodulatory effects, further research is needed to standardize intervention protocols and optimize their clinical applicability.[5–8,16,24] In this context, the present study aims to evaluate and compare two neural potentiation protocols with different electrical stimulation parameters, on the basis of the hypothesis that both may lead to improvements in muscle performance. Specifically, the primary objective was to assess whether a single session of US-guided PNM applied to the median nerve induces immediate changes in maximal handgrip strength in healthy adults, and whether one protocol yields statistically superior outcomes. As a secondary objective, the study sought to determine whether there were differences in perceived pain intensity between the two protocols during the intervention. This work will advance knowledge of the application of US-guided PNM in neuromuscular potentiation and its potential implementation in sports physiotherapy and therapeutic exercise, thereby consolidating this technique as a promising, evidence-informed tool within invasive physiotherapy.

## MATERIALS AND METHODS

### Study Design

A randomized, evaluator- and participant-blinded clinical trial was conducted to assess the effects of two US-guided PNM protocols on maximal handgrip strength in healthy volunteers. Because both groups received active PNM interventions, and no standard, sham, or reference condition was included, the study was designed with two experimental groups rather than a true control group.

The study was conducted at Fisiocete Clinic in Porto, Portugal. It was approved by the ethics committee of San Pablo CEU University (1000-25) and complied with the principles established in the Declaration of Helsinki. It was registered on ClinicalTrials.gov (reference: NCT07098130). All participants gave written informed consent. They were informed that their participation was voluntary and that they had the right to withdraw at any time. Data confidentiality and anonymization also were assured.

### Participants and Sample Size

Patient recruitment was performed at Fisiocete Clinic in Porto (Portugal). To be included in the study, participants had to meet the following inclusion criteria: (1) aged 18 to 45 years and (2) absence of musculoskeletal injuries that could affect their physical condition. Exclusion criteria for the study included: (1) previous upper limb and/or cervical spine surgery, (2) presence of painful conditions during measurements, (3) diagnosis of neurologic pathology, (4) current use of drugs, and (5) specific contraindications to US-guided PNM, including electrophobia, belonephobia, pregnancy, epilepsy, or the presence of a pacemaker.

The sample size was calculated using a pretest power analysis, based on the classical formula for comparing means between two independent groups, derived from the normal distribution and based on the *t*-test:

$$n = 2\,(Z\alpha/2 + Z\beta)^2 \cdot SD^2 \,/\, (\text{Expected difference})^2$$

For this calculation, data from the randomized controlled trial by Martín-Caro Álvarez et al[27] were used as a reference, given that study evaluated maximal handgrip strength in healthy subjects after US-guided PNM of the median and ulnar nerves. In that study, handgrip strength baseline SD values were extracted from the published figure using the WebPlotDigitizer software (v4.8, Automeris LLC) and pooled across groups, yielding a pooled baseline SD of 9.76 units. This value was used as the estimate of variability for the sample size calculation. On the basis of this variability, a between-group difference of six units was assumed, with a two-sided significance level of $\alpha = 0.05$ and an 80% statistical power ($\beta = 0.20$). Under these assumptions, the required sample size was estimated at 43 participants per group, yielding a total planned sample of 86 participants. Given that the present study evaluated immediate pre–post effects after a single intervention session without follow-up, participant attrition was not expected, and no additional adjustment for potential dropouts was applied.

## Randomization and Blinding

Group allocation was randomized by an independent third party using a simple randomization method. Specifically, colored balls (green for group protocol 1 and red for group protocol 2) were placed in an opaque bag and drawn one at a time for each participant to ensure random allocation. The study followed a triple-blind design in which the evaluator, the participants, and the statistical analyst were blinded to group allocation.

## Study Variables

### Sociodemographic Variables

Sociodemographic data collected for each participant included sex, age, weight, height, and dominant arm. Subsequently, body mass index (BMI) was calculated using the standard formula: BMI = weight (kg)/height ($m^2$).

### Primary Variable

The primary variable was the maximal handgrip strength using a digital handgrip dynamometer (Digital Kern & Sohn MAP 80K1S, KERN & SOHN GmbH, Balingen-Frommern, Germany).[28–30] Maximal handgrip strength, assessed using a hand-held dynamometer, is widely recognized as a valid and reliable measure of maximal voluntary grip force. Studies have reported excellent test–retest and interrater reliability, with intraclass correlation coefficients ranging from 0.90 to 0.97 for devices similar to that used in this study.[31,32]

Maximal handgrip strength was measured in kilograms (kg) and recorded before and immediately after the intervention by an independent evaluator blinded to group allocation. Participants were seated with their backs straight, feet flat on the floor, and forearms resting on a horizontal surface, ensuring a 90° angle at the elbow (Fig. 1). Before starting the measurements, participants were instructed in the use of the digital handgrip dynamometer. The participants were requested to perform a maximal voluntary isometric contraction lasting 3 seconds with their dominant hand. Three trials were completed with 30-second rest intervals, and the mean of the three peak values across the three trials was used for analysis.[33]

### Secondary Variable

The secondary variable was pain intensity during the US-guided PNM intervention, measured with the Numerical Pain Rating Scale (NPRS), where 0 indicates “no pain” and 10 means "worst imaginable pain.”[34]

**Figure 1.** Participant positioning for maximal handgrip strength assessment. [Color figure can be viewed at www.neuromodulationjournal.org]

## Intervention

The interventions for both groups (protocol 1 and protocol 2) were performed by an experienced physiotherapist with two years of experience in US-guided PNM. During the intervention, subjects were placed supine, with their dominant upper limb extended and externally rotated. Before the intervention, the treatment area was cleansed with chlorhexidine. Next, the median nerve was located with US guidance (VINNO E35, 10–15 MHz linear transducer, Suzhou, China), approximately 5 cm proximal to the medial epicondyle, with the transducer positioned in a transverse orientation for optimal visualization. A 30-mm × 0.30-mm filiform, solid needle (Tewa, Pullach, Germany) was inserted using an in-plane, long-axis approach, from lateral to medial, placing the tip as close as possible to the epineurium of the median nerve (Fig. 2). The needle remained in the same position throughout the procedure.

Subsequently, a single session of US-guided PNM was delivered using a specifically developed and medically certified device (EPTE Bipolar System, Ionclinics, Sevilla, Spain), according to the group allocation: (1) protocol 1: 10 seconds of stimulation with symmetrical biphasic current at 10 Hz, pulse width of 250 μs, followed by 10 seconds of rest, for ten cycles,[15] and (2) protocol 2: 5 seconds of stimulation with symmetrical biphasic current at 100 Hz, pulse width of 350 μs, followed by 55 seconds of rest, for five cycles.[7] For

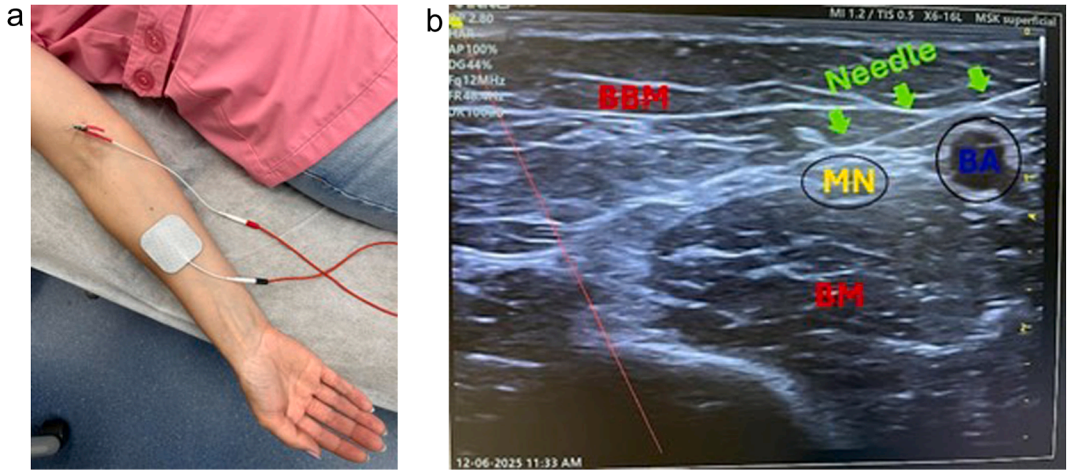


**Figure 2.** Positioning of the needle and US-guided targeting of the median nerve during percutaneous neuromodulation. a. Needle placement on the participant. b. US view confirming proximity to the target nerve structure. BA, brachial artery; BBM, biceps brachii muscle; BM, brachialis muscle; MN, median nerve. [Color figure can be viewed at www.neuromodulationjournal.org]

both stimulation protocols, intensity was individualized before the experimental stimulation cycles. A continuous test stimulation at the same frequency as the experimental protocol was first applied and progressively increased until a clear, visible muscle contraction was achieved within the maximal tolerable, nonpainful range reported by the participant. Once established, this intensity was kept constant throughout all stimulation cycles of the respective protocol.

### Statistical Analysis

Statistical analysis was performed using R Studio (version 2024.12.0). A significance level of 0.05 was established for all tests. Quantitative variables are expressed as mean and SD, whereas qualitative variables are expressed as frequencies and percentages. Before analyzing the primary outcome variable (maximal handgrip strength), the assumptions of normality and homogeneity were evaluated. Data distribution was assessed using the Shapiro-Wilk test, histograms, and Q-Q plots. Although preintervention values showed a statistically significant deviation from normality ($p = 0.016$), visual inspection revealed no substantial violations. The hypothesis of homogeneity of variances between groups was confirmed using Levene's test ($p = 0.247$). In addition, a derived variable representing the change in strength (Δ strength = post − pre) was calculated, and its normality within each group was assessed, showing acceptable normal distributions (protocol 1: $p = 0.334$; protocol 2: $p = 0.104$). All of this, together with the sample size ($N = 86$) being supported by the central limit theorem, justified the application of parametric methods. Specifically, a two-way mixed design analysis of variance (ANOVA) was performed to evaluate the effect of the intervention on maximal handgrip strength. The model included a between-groups factor (Group: protocol 1 vs protocol 2), a within-groups factor (Time: pre- vs post-intervention), and the interaction term between these two factors (Group × Time). The analysis was performed using type III sum of squares, and post hoc pairwise comparisons were conducted using estimated marginal means.

For the secondary outcome variable (perceived pain intensity during the stimulation), only between-groups differences were assessed. This variable was treated as a discrete ordinal variable because although it uses numerical values, this scale reflects subjective perception, in which the distance between scores is not guaranteed to be equal (eg, the perceived difference between 0 and 1 may not be the same as between 6 and 7). Given this noninterval nature and the limited number of distinct levels observed in the data set (values ranging only from 0–4), it was considered inappropriate to treat the variable as continuous or normally distributed. Therefore, nonparametric methods were used to analyze this variable. Specifically, the Mann-Whitney *U* test (also known as the Wilcoxon rank-sum test) was applied. In addition, to quantify the magnitude of the observed effects, effect sizes were calculated using Rosenthal's *r* coefficient. According to Fritz et al,[35] values <0.10 are considered negligible, between 0.10 and 0.29 indicate a small effect, between 0.30 and 0.49 a moderate effect, and values of ≥0.50 a large effect.

## RESULTS

A total of 86 participants, evenly distributed between the two intervention groups ($n = 43$ in protocol 1 and $n = 43$ in protocol 2), completed the study and were included in the final analysis (Fig. 3).

The sample comprised 86 healthy adults with a mean age of 30.90 ± 7.61 years. Participants in protocol 1 had a mean age of 31.23 ± 7.45 years, whereas those in protocol 2 had a mean age of 30.56 ± 7.85 years. Regarding sex distribution, 65.1% of participants (56) were male, and 34.9% (30) were female. Protocol 1 included 60.5% men (26) and 39.5% women (17), whereas protocol 2 included 69.8% men (30) and 30.2% women (13). The overall BMI was 24.31 ± 2.95 kg/m$^2$, with comparable values across groups (protocol 1: 24.76 ± 3.45 kg/m$^2$; protocol 2: 23.85 ± 2.31 kg/m$^2$).

Concerning maximal handgrip strength, the two-way mixed design ANOVA analysis revealed no statistically significant differences either between groups (protocol 1: 10 Hz vs protocol 2: 100 Hz) or within groups (pre vs post). Descriptive pre- and post-intervention values for maximal handgrip strength, along with the full ANOVA results and post hoc pairwise comparisons, are

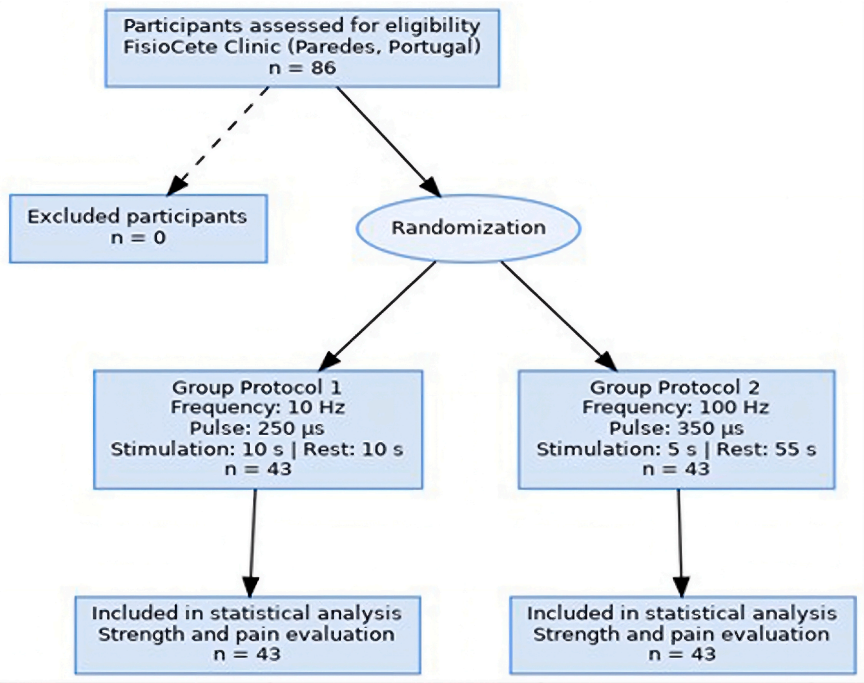


**Figure 3.** Participant flow diagram. [Color figure can be viewed at www.neuromodulationjournal.org]

presented in Table 1. Moreover, Figure 4 illustrates the distribution of maximal handgrip strength values for each intervention group at both measurement timepoints.

In addition, given the absence of significant between-group differences, a post hoc power analysis was conducted to assess the robustness of the negative findings. On the basis of the observed pooled SD of 3.18 kg for changes in maximal handgrip strength and the final sample size ($n = 43$ per group), the study had 80% power to detect between-group differences of ≥1.37 kg (Cohen's $d = 0.43$). The observed mean difference (0.34 kg; Cohen's $d = 0.11$) was well below this threshold, suggesting that any true effect between protocols, if present, would be very small and of limited practical relevance.

Regarding the secondary variable (perceived pain intensity during the intervention), no statistically significant differences were found ($p = 0.068$), with a small effect size ($r = 0.197$). Although this value approached the threshold for statistical significance, the actual mean difference in pain experience between the two protocols was minimal (1.56 ± 1.24 in protocol 1 vs 2.00 ± 1.02 in protocol 2). The distribution within each intervention group is shown in Figure 5.

## DISCUSSION

This study aimed to compare the effects of two US-guided PNM protocols applied to the median nerve on maximal handgrip strength in healthy adults. Despite previous evidence suggesting the potential of electrical stimulation to induce strength gains and modify neuromuscular excitability, the results showed no immediate changes in maximal handgrip strength across any of the protocols.

Several studies have indicated beneficial effects of US-guided PNM on muscle function and neuromuscular performance across different populations and nerve targets.[5,8,13,16,36] Femoral nerve stimulation has been associated with increases in maximal isometric quadriceps strength[16] and with improvements in vertical jump performance and squat execution speed.[5] Moreover, sciatic nerve stimulation has produced significant gains in hamstring strength and power,[13] in addition to increases in hip muscle strength.[36] Furthermore, tibial nerve stimulation has been shown to induce immediate improvements in balance and flexor hallucis longus endurance.[8] Altogether, these findings highlight the potential of the US-guided PNM to enhance neuromuscular performance across different populations and nerve targets.

However, as in the present study, other research has not identified significant increases in strength after isolated application of US-guided PNM. In fact, Beltrá et al[19] analyzed various stimulation protocols and reported a decrease in strength across all conditions, including placebo, with a significantly greater reduction observed with continuous low-frequency stimulation, despite sensorimotor changes. Similarly, Martín-Caro Álvarez et al[27] reported a transient decrease in maximal handgrip strength after low-frequency US-guided PNM of the median and ulnar nerves. In the sports setting, Sangiacomo et al[12] applied US-guided PNM to the axillary and suprascapular nerves in CrossFit athletes and observed improvements within the experimental group, although without significant differences from the control group (no intervention). Álvarez et al[14] showed that higher frequencies could modify cortical and spinal excitability without producing functional changes in isometric strength, underscoring the complexity of the neuromodulatory response in populations without prior deficits.

The literature review reveals that several methodologic and physiologic factors decisively influence the effects of US-guided

**Table 1.** Comparative Effects of Two US-guided PNM Protocols (10 Hz vs 100 Hz) on Maximal Handgrip Strength.

| Outcome | Protocol 1 (10 Hz) | Protocol 2 (100 Hz) | ANOVA results (*p*-value) | Post hoc pairwise comparisons (*p*-value) |
|---|---|---|---|---|
| **Preintervention (kg)** | 40.09 ± 12.16 | 42.19 ± 11.56 | Group effect (between-group differences): 0.376 | Comparisons of groups: |
| **Postintervention (kg)** | 39.89 ± 12.75 | 42.33 ± 11.10 | Time effect (within-group differences): 0.921 | 0.412 (preintervention) |
| **Δ Pre–post (kg)** | −0.20 ± 3.25 | 0.14 ± 3.10 | Group × time interaction: 0.592 | 0.348 (postintervention) |
| | | | | Within-group comparisons: |
| | | | | 0.653 (protocol 1) |
| | | | | 0.757 (protocol 2) |

Values are expressed as mean ± SD. Δ Pre–Post indicates the change in maximal handgrip strength after the intervention. ANOVA results correspond to a two-way mixed-design ANOVA. Post hoc pairwise comparisons were conducted using estimated marginal means.

PNM, including the muscle group stimulated, the current frequency, the number of sessions, and the participant's initial functional condition.[5–9,11,14,19,27] These elements may explain the heterogeneity of results across studies. One of the most relevant is the muscle group targeted. Evidence suggests that US-guided PNM tends to produce more consistent and measurable improvements when applied to lower-limb nerves and larger muscle groups. Gallego-Sendarrubias et al[5] reported improvements in jump performance, whereas De la Cruz-Torres et al[8] observed immediate activation changes in the flexor hallucis longus; similarly, Martín et al[13] documented increases in hamstring strength and power. These studies suggest greater responsiveness of the lower-limb musculature, possibly due to larger muscle mass, greater motor unit recruitment capacity, or specific fiber-type composition. In contrast, stimulation of smaller or more specialized muscles, such as those involved in handgrip strength, as in the present study, may yield subtler or nondetectable changes, which aligns with the more modest responses reported in upper-limb interventions in the available literature.[12,14,19,27,37]

Another key aspect is the stimulation frequency, which is widely recognized as a modulator of neuromuscular effects. Martín-Caro Álvarez et al,[27] when applying 10-Hz stimulation to the median and ulnar nerves, not only failed to observe improvements but also observed a significant decrease in performance, indicating a possible transient inhibitory effect. Beltrá et al[19] corroborated that variations in frequency and pulse width produce diverse sensorimotor responses, reinforcing the idea that frequency is a critical parameter. Similarly, Sangiacomo et al,[12] when applying 100 Hz to the shoulder in athletes, also found no between-group differences, despite individual improvements. However, Serrano-Muñoz et al[37] indicated that transcutaneous stimulation with high-frequency alternating current (10 kHz) significantly reduced maximal handgrip strength during and after application, possibly owing to reversible motor conduction blockade. Moreover, Álvarez et al[14] observed that alternating currents at 10 kHz and 20 kHz applied to the median nerve modulated spinal excitability and suppressed motor-evoked potentials, without producing immediate functional

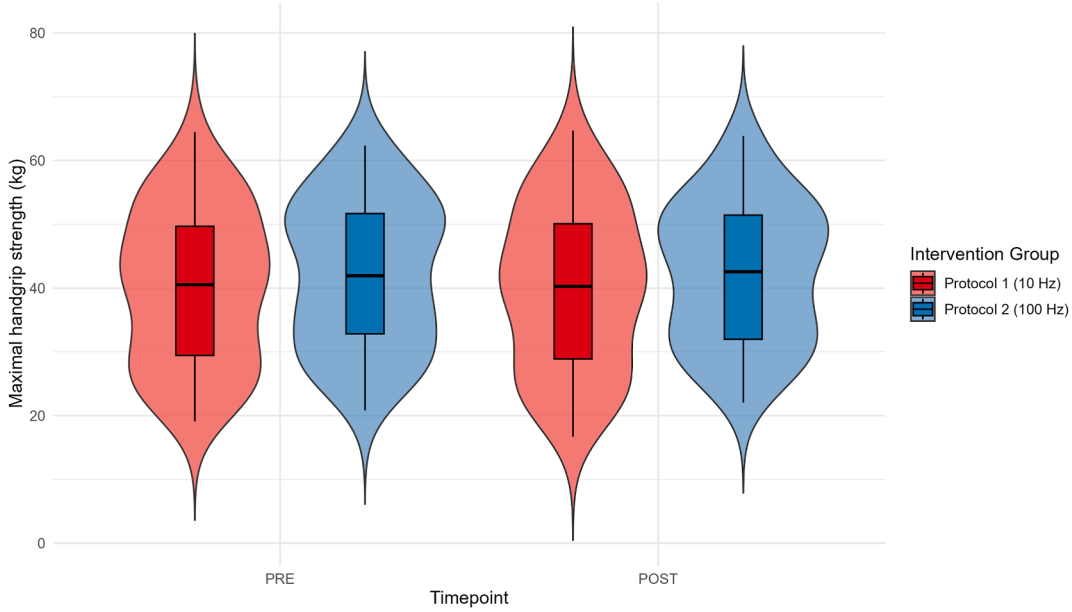


**Figure 4.** Box and violin plot showing maximal handgrip strength before and after the intervention in protocol 1 (10 Hz) and protocol 2 (100 Hz). Median values, interquartile ranges, and full data distribution are displayed. [Color figure can be viewed at www.neuromodulationjournal.org]

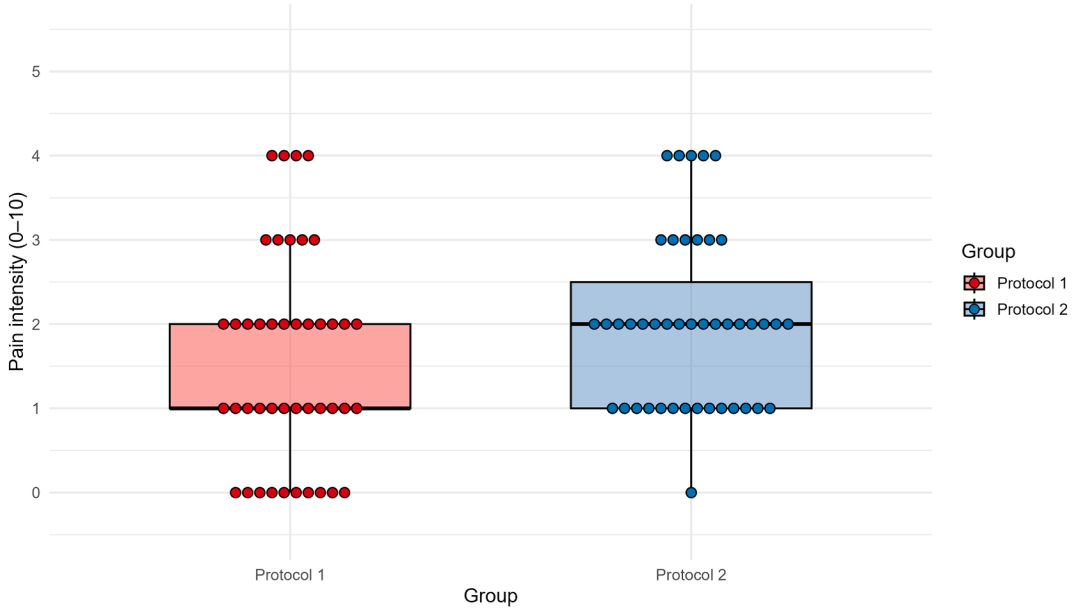


**Figure 5.** Box plot comparing the pain intensity perceived during the intervention in protocol 1 (10 Hz) and protocol 2 (100 Hz). Individual data points are shown, along with median values, interquartile ranges, and possible outliers. [Color figure can be viewed at www.neuromodulationjournal.org]

improvements. These studies show that low frequencies (≈10 Hz) primarily activate Aα motor fibers, producing visible contractions and a facilitatory effect, whereas high frequencies (10–20 kHz), especially in alternating current, act on Aβ and Aδ sensory fibers, modulating the sensorimotor response through reversible inhibitory mechanisms.[14,37] Overall, the studies agree that neither low nor high frequencies produce immediate functional improvements in healthy subjects, even with maximum tolerated intensities and stimulation of major motor nerves.[19,27,37]

Another relevant factor is the number of sessions. In clinical settings, several authors have shown that multiple sessions are essential to achieve lasting relief in pain or improvement in strength. Beltrá et al[19] suggest that repeated stimulation is necessary to consolidate sensorimotor modulation. Requena et al[6] described posttetanic potentiation phenomena after repeated quadriceps stimulation, and Álvarez et al[14] indicated that a single high-frequency session was insufficient to induce measurable changes in muscle strength. Although some studies have reported functional improvements after two sessions of US-guided PNM combined with training,[5] evidence for significant gains in maximal strength with so few applications remains scarce. Most of the strength gains reported in the literature derive from protocols involving multiple sessions over days or weeks[6,19] or from different types of electrical stimulation. Future studies should use longitudinal designs with multiple sessions, enabling analysis of response curves and cumulative effects.

The participants' baseline functional condition also should be considered. Despite the application of maximum tolerated intensities, no significant improvements in maximal handgrip strength were recorded, possibly owing to a ceiling effect, which also was reported by Sangiacomo et al[12] in CrossFit athletes. When comparing baseline handgrip strength values with the normative values of Mathiowetz et al[38] and Wang et al,[39] it was observed that the mean values in our sample were very close to those expected for their age and sex. Specifically, women (mean age 32.2 years) presented a baseline handgrip strength of 28.5 kg, compared with a normative values of approximately 28.9 kg. Similarly, men (mean age 29.9 years) showed a mean baseline values of 47.9 kg, which falls within the expected normative range for this age group (46.5–49.7 kg), despite the transition between age categories at 30 years. This high baseline performance may have limited the detection of further improvements.

In addition, studies with participants who had a clinical condition showed positive effects on muscle strength gains. San-Emeterio-Iglesias et al[36] observed increases in hip muscle strength after sciatic nerve stimulation in patients with chronic low back pain, and Álvarez-Prats et al[16] reported improvements in isometric quadriceps strength after femoral nerve stimulation in subjects with preexisting dysfunction. These findings contrast with the absence of change observed in healthy participants and support the idea that neuromuscular alterations, even subclinical ones, may promote a more effective response to electrical stimulation by facilitating the reactivation of inhibited or underused motor units.

In contrast, pain perception during the intervention was assessed using the NPRS as a secondary outcome. In both protocols, the reported levels were low, showing good tolerance to the technique and supporting its clinical viability, without interfering with the patient experience or the efficacy of the procedure. A possible explanation for these data lies in the individualized dosing approach adopted in this study; the intensity was individualized to induce a visible muscle contraction while remaining within a well-tolerated, nonpainful range. This result coincides with that reported by Fidalgo-Martin et al,[1] who, in their systematic review, highlighted that US-guided PNM presents a high safety profile and few adverse effects within the field of neuromodulation.

Several limitations must be acknowledged. A primary limitation relates to the characteristics of the study sample. The participants were young, healthy, and physically active adults with high baseline handgrip strength, making it difficult for the US-guided PNM interventions to produce additional measurable improvements.

Consequently, these results may be limited to this young and healthy population and cannot be generalized to the broader population. Future studies with broader age ranges and diverse functional profiles should determine whether populations with greater improvement potential show more pronounced effects. Future research also may benefit from incorporating neurophysiologic assessments to better elucidate the mechanisms underlying potential strength changes.

Another important constraint lies in the intervention design. Only a single session of US-guided PNM was administered, which may have been insufficient to induce neuroplastic adaptations. Evidence suggests that repeated applications are typically required to elicit lasting sensorimotor adaptations. Future research should explore multisession interventions to assess cumulative and sustained effects. A further limitation of this study is the absence of a placebo or control group. Although the lack of significant findings reduces the impact of this issue, nonspecific factors such as placebo or expectancy effects cannot be completely excluded and may have interacted with the intervention effects.

Furthermore, the intervention targeted a relatively small, functionally specialized muscle group (hand flexors) whose responsiveness may differ from that of muscles with greater motor recruitment and biomechanical relevance. Moreover, assessment also was restricted to the dominant limb, without considering potential contralateral or cross-effects. Incorporating bilateral measurements in future studies would provide a more comprehensive understanding of potential central or systemic neuromodulatory responses.

Finally, although stimulation parameters such as frequency and intensity were standardized, the study lacked both a long-term follow-up and comparisons of different stimulation protocols or dosing strategies. This highlights the necessity of longitudinal studies with broader methodologic designs across more diverse populations, including clinical cohorts with neuromuscular dysfunction such as muscle weakness or other motor impairments.

## CONCLUSIONS

A single session of US-guided PNM did not produce statistically significant immediate changes in maximal handgrip strength in healthy adults regardless of the protocol used. Pain perception during the application of the technique was low in both protocols, confirming that the technique is well-tolerated and safe.

### Authorship Statements

Hugo Miguel Barbosa da Silva, Fermín Valera-Garrido, Francisco Minaya-Muñoz, David Álvarez-Prats, and Óscar Carvajal-Fernández were responsible for the study conceptualization. Hugo Miguel Barbosa da Silva, Pablo Herrero, and Óscar Carvajal-Fernández were responsible for the study methods. Diego Lapuente-Hernández and Alberto Carcasona-Otal were responsible for the data curation and formal analysis. Hugo Miguel Barbosa da Silva and Óscar Carvajal-Fernández were responsible for writing and preparing the original draft. Fermín Valera-Garrido, Francisco Minaya-Muñoz, David Álvarez-Prats, Diego Lapuente-Hernández, Pablo Herrero, and Alberto Carcasona-Otal were responsible for review and editing the manuscript draft. All authors have read and agreed to the published version of the manuscript.

### Conflict of Interest

The authors reported no conflict of interest.

**How to Cite This Article**

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## COMMENTS

In this preregistered randomized clinical trial, Barbosa et al partially replicate and extend the results of previous studies investigating the effects of percutaneous peripheral nerve stimulation (pPNS) applied on the median nerve on the grip strength of healthy volunteers. Here, the findings of similar previous studies[7,19] are not only replicated in a larger sample size, but a new protocol also is studied (intermittent 10 Hz). In my opinion, the present study strengthens what is known about pPNS effects in maximal strength.

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This is an interesting manuscript with a good, reasoned review of previous studies that highlights the conflicting results of this technique in clinical practice and the critical points that need to be resolved for its effective use.

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