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Review

Neuromuscular Electrical Stimulation Improves Muscle Strength, Biomechanics of Movement, and Functional Mobility in Children With Chronic Neurological Disorders: A Systematic Review and Meta-Analysis

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Abstract

Objective: Chronic neurological disorders (CNDs) generally produce deleterious effects on the musculoskeletal system and can affect physical activity and increase sedentary behavior in children, hindering the execution of training programs and the attainment of a correct dose of exercise. The purpose of this systematic review was to analyze the effect of neuromuscular electrical stimulation (NMES) on skeletal muscle and then on biomechanics of movement, functional mobility, strength, spasticity, muscle architecture, and body composition of children and adolescents with CNDs and chronic diseases.
Methods: The search was conducted in April 2020 in PubMed, MEDLINE, Scopus, the Cochrane Library, and Web of Science, without publication period restriction. Publications investigating the effect of NMES on children and adolescents with CNDs and other chronic diseases were independently selected by 2 researchers. One author independently extracted data from the studies selected, and a second author cross-checked.
Results: Eighteen studies with 595 participants aged between 3 and 14 years were included. Quality assessment showed that 50% of the studies presented a low risk of bias. The pooled effect of NMES on gross motor functional measure, calculated as a standardized mean difference using a random effects model, was 0.41 (95% CI = 0.19–0.64).
Conclusion: The use of NMES programs for children diagnosed with cerebral palsy, spinal muscular atrophy, and obstetric injury of the brachial plexus was effective in improving muscle strength, biomechanics of movement, and functional mobility.
Impact: NMES can be a useful tool to prevent the reduction of mobility that results from CNDs.

Keywords: Adolescent, Child, Chronic Disease, Electric Stimulation Therapy, Muscle Strength

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Introduction

Chronic neurological disorders (CNDs) affect the communication of the central and/or peripheral nervous system, which generally produces effects on the musculoskeletal system and a decrease in muscle mass and strength.[1] Thus, they impact children's health status and growth.[2]

Disorders such as cerebral palsy, spinal muscular atrophy, and obstetric brachial plexus injury are clear examples of CNDs that are produced before and during birth or childhood.[3] These conditions can alter kinetic chains,[4] either due to the direct effects of the disease (symptoms and treatments) or indirect effects (prolonged hospitalizations and restricted physical activities).

Physical abilities are linked to the cardiovascular and strength levels of the child[5,6] and are associated with increased morbidity and mortality.[7] Thus, appropriate and early interventions are key for good clinical evolution in CNDs. Physical exercise has been shown to be the best strategy to alleviate the adverse effects,[8,9] improving cardiovascular and musculoskeletal fitness, neurological development, mental health, and reducing cardiometabolic risk factors.[10]

CNDs can affect physical activity and increase sedentary behavior in children, hindering the correct dose of exercise and the execution of training programs. In these cases, neuromuscular electrical stimulation (NMES) is presented as a useful tool to prevent muscle atrophy and the reduction of mobility that results from chronic diseases.[11,12] NMES consists of stimulating the muscles through electrical currents at a certain frequency, transmitted through superficial electrodes placed on the target muscles, producing medium-to-high–intensity neuromuscular work without the need to use an external load.[13] It can be used in isolation or associated with exercise. Physical improvement derived from NMES can have a significant impact on muscle, and more specifically on muscle strength,[14,15] biomechanics of movement,[16] spasticity,[17] muscle architecture,[18] body composition,[19] and functional mobility[20] related to daily life, contributing to improving child development.[21] Despite the usefulness of NMES in improving different functional capacities related to health in adults,[22] the effectiveness of this tool for muscle function has not yet been determined in children with chronic diseases or with CNDs. Thus, the aim of this systematic review was to analyze the effect of NMES on skeletal muscle and, consequently, on biomechanics of movement, functional mobility, muscle strength, spasticity, muscle architecture, and body composition of children and adolescents with CNDs and chronic diseases.

Methods

Data Sources and Searches

The search was conducted in April 2020 on PubMed, MEDLINE, Scopus, the Cochrane Library, and the Web of Science, without publication period restriction. The search was restricted to studies written in English. A combination of the following terms was used: "[(Neuromuscular electrical stimulation or NMES) and (Child∗ or Adolescent)] and (Muscle)". The term "muscle" was included to limit studies to NMES application on muscles, focusing on improvements in muscle strength, motor control, and spasticity, among others. All the results were saved for later reporting. Gray literature and reviews were excluded. Gray literature is defined as unpublished documents, or those that were published but distributed through unconventional channels (eg, doctoral theses, conference proceedings, research reports, memoirs, and projects), which usually poses special search and locating problems for the research community.

Study Selection

The systematic review followed the items from Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.[23] The protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO registration number: CRD42020177651) before the data search started.

The inclusion criteria selected were: (1) diagnosis of a CND or chronic disease; (2) age between 1 and 17 years; (3) use of surface electrodes (above the skin); (4) presence of a control group; (5) skeletal muscles treated with NMES; and (6) publication as a journal article. Exclusion was applied when the studies included: (1) adult participants; (2) percutaneous electrodes; (3) nonperipheral muscles; and (4) functional electrical stimulation. Two authors (F.C-V. and A.F.S.J.) independently reviewed the titles and abstracts of the studies, selected those that met the inclusion criteria and extracted the data. In case of disagreement, another author (E.L-Z.) also reviewed and discussed the article until a consensus was reached. All decisions were tracked using a spreadsheet.

Data Extraction and Quality Assessment

One author (F.C-V.) independently extracted data from the studies selected and a second author (A.F.S.J.) cross-checked. In case of disagreement, another author (E.L-Z.) also reviewed the data until a consensus was reached. The following information was extracted from the articles: metadata (authors names, publication year, and country); methods (study design, sample size, randomization details, and group assignment); sociodemographic characteristics of participants (age and sex); measured outcome variables; inclusion and exclusion criteria; recruitment method; control group description; and treatment group interventions (types of interventions, duration, frequency, intensity, and dose). Mean and SD at baseline and postintervention, or changes in reported outcome variables, were recorded for control and intervention groups. When the SD was not available, we computed it from the SE. When median and interquartile range (IQR) were reported, we estimated the sample mean and SD from the sample size, median, and IQR, as described elsewhere.[24] If a study reported multiple interventions, each group was recorded separately. When information was presented graphically, mean and SD were calculated from the available data in the figures using the measurement tools of a commercially available raster graphics editor. Otherwise, authors were contacted in the event of unreported data.

To assess the quality of individual studies, because we found some diversity in the study designs (ie, not just randomized controlled trials [RCTs]), we adapted the revised Cochrane risk-of-bias tool for randomized trials (RoB 2).[25] Because the original RoB was designed for RCTs only, the purpose of the adaptation was to make it suitable for assessing studies with non-RCT designs and still provide valuable information on their quality. The RoB-derived items to assess risk of bias were: (1) bias derived from the randomization process, (2) bias due to deviations from planned interventions, (3) bias

due to missing data results, (4) bias in the measurement of the result, and (5) bias in the selection of the reported result. Two investigators (F.C-V. and A.F.S.J.) conducted separate risk-of-bias assessments. In case of disagreement, a third author (E.L-Z.) also evaluated the study, and the disagreement was resolved by consensus. First, the scoring of risk-of-bias items was determined as follows: 1 point for low risk, 0 points for some concerns, and −1 point for high risk. Consequently, the overall scores ranged from −5 to 5. To categorize this score, the following benchmarks were used: (1) *High risk of bias:* between −5 and 1 points (ie, 2 or more domains presenting high risk of bias); (2) *Some concerns:* between 2 and 3 points (ie, only 1 domain presenting high risk of bias); and (3) *Low risk of bias:* between 4 and 5 points (ie, at least 4 domains presenting low risk of bias).

Data Synthesis and Analysis

Pre- and postintervention data were used to calculate mean differences and pooled SDs. Then, Hedges *g* and its 95% CI were computed to estimate the standardized mean differences between control and treatment, which might be interpreted in the same way as Cohen *d*: 0.20, small; 0.50, medium; 0.80, large.[26] We used the equations recommended by Borenstein et al.[27]

When at least 4 groups reported the same outcome, meta-analyses were conducted with the metan[28] command for Stata using random-effects models, under the assumption of variability of true effects between studies (eg, variability in study designs, participant characteristics, and protocols). The percentage of variation across studies due to heterogeneity rather than chance was assessed using the I^2 statistic and its 95% CI. Additionally, we assessed publication bias by visually inspecting funnel plots[29] and applying the Egger test, computing a linear regression of the intervention effect estimates on their SEs.[30] Significance level was set at .05. All statistical analyses and plots were performed using Stata 15.1 (StataCorp, College Station, TX, USA).

Role of the Funding Source

The funders played no role in the design, conduct, or reporting of this study.

Results

Study Selection

Eighteen studies (15 RCTs, 2 non-RCTs, and 1 cross-sectional study) were selected for the qualitative analysis (Fig. 1).[31–48] We decided to include in the present systematic review the study of Elbasan et al[37] because, although it presented a cross-sectional design, randomization, a control group, and low risk of bias were found (Fig. 1).

Finally, 6 articles included valid data for the quantitative analysis and were used in the meta-analysis.[32,37,43,44,47,48]

Study Characteristics

Participants

The total number of participants was 595, aged between 3 and 14 years, of which 49% were girls. The majority of the studies (88.9%) were about cerebral palsy (16 articles), 5.6% were about spinal muscular atrophy (1 article), and the remaining 5.6% were about obstetric brachial plexus injury (1 article). The number of participants in each study varied considerably, from 6 to 100 subjects. The tests most used to characterize the sample of patients were the Modified Ashworth Scale (38.9%), the Gross Motor Function Classification System (22.2%), and the Zancolli Scale (11.1%).

Quality

From the 18 studies included, 83.3% were RCTs (ie, 15 studies), 11.1% were non-RCTs (ie, 2 studies), and 5.5% were cross-sectional studies (ie, 1 study). The assessment of bias is presented in Table 1. Half (50%) of the studies analyzed presented a low risk of bias.

Variables Measured

The effects of NMES were studied in distinct body segments, including lower limb (61.1%), upper limb (27.8%), and back-trunk (11.1%). There was no consensus regarding the variables analyzed in the different studies, which made it difficult to use all the selected studies in the quantitative analysis.

As previously described in the objective of the present review, the findings were distributed into 5 categories describing 5 muscle and physical health-related components: (1) biomechanics of movement, (2) functional mobility related to physical activities of daily life, (3) muscle strength, (4) spasticity and muscle architecture, and (5) body composition.

Interventions

We analyzed studies using NMES programs from 4 to 48 weeks, with an average application of 14 weeks. All the programs used NMES as their main intervention. Frequencies ranged from 20 to 35 Hz, and the intensity applied during NMES ranged from 20 to 100 mA. The programs were applied at home in 50% of studies, in rehabilitation centers in 27.8%, and were not reported in 22.2% of the studies. In 50% of the cases, NMES was described as being applied by professionals, with an explanatory session used in only 33.3% of the studies, and a follow-up in 16.7%. NMES was used alone in 16.7% of the studies, as well as in association with exercise (16.7%), physical therapy (33.2%), occupational therapy (16.7%), and neuropathic rehabilitation and treatment (ie, administration of botulinum toxin and/or exercises focused on the stimulation and facilitation of the communication of the nervous system: 16.7%).

As we have shown before, 88.9% of the NMES interventions were for cerebral palsy, 5.6% for spinal muscular atrophy, and the remaining 5.6% for obstetric brachial plexus injury. For more details see Tables 2–5.

Effect of Intervention

Biomechanics of Movement

Improvements in range of motion (ROM) were observed in most of the studies analyzed,[31,32,41–45] except for four[42,43,45,46] (Tab. 2). Improvements in the dorsal kyphosis angle were demonstrated for the spine ROM.[32] As for the upper limbs, 1 article found increases in wrist active ROM.[41] In addition, for the lower limbs ROM, improvements were observed in ankle dorsiflexion,[42] the knee genu recurvatum,[44] and knee hyperextension.[44] However, a few studies did not find any significant increase for ankle ROM,[45] knee popliteal angle,[42,46] or knee flexion during gait.[45]

Regarding the biomechanical variables related to gait, 2 studies found significant improvements for walking speed,[43,47] although 1 of them[47] observed a decrease after 3 weeks of follow-up without NMES. Moreover, interventions

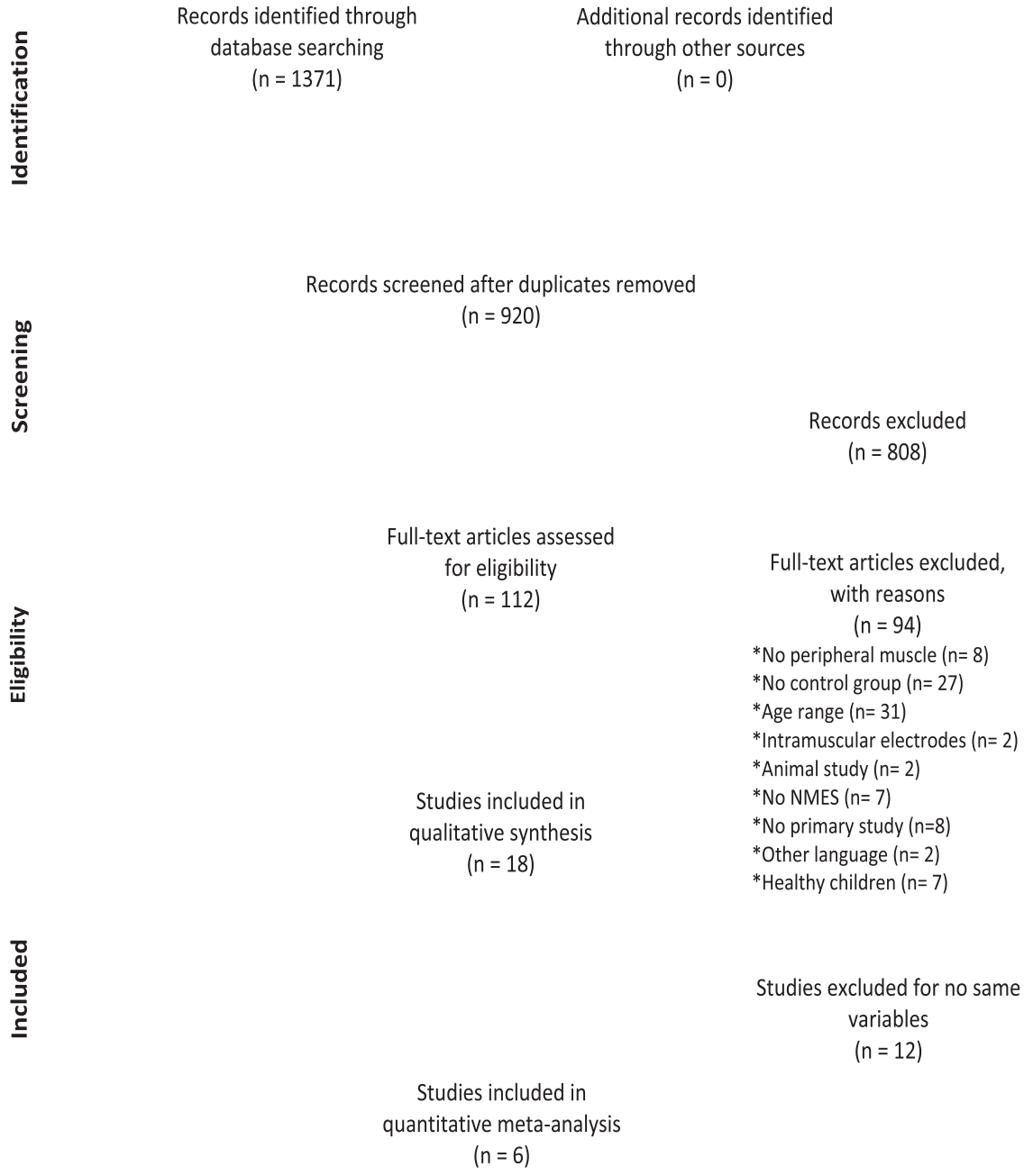

Figure 1. Flow of studies through the review.

with NMES increased length and step width,[31] cadence,[43] and improved the global selective motor control measured in the lower limbs,[34] and increased significantly the Physician Rating Scale.[45] In contrast, some authors did not report significant improvements for walking speed,[42,45] cadence, and step length.[43,45] Furthermore, when the crouch gait was evaluated,[42] a significant improvement was found.

Functional Mobility

Twelve studies[32–38,43–45,47,48] found a significant increase, and only two[41,43] did not find any improvement in the variables measured (Tab. 3). Regarding the use of NMES applied to the spine, 2 studies showed improvements using the Gross Motor Functional Measure (GMFM; ie, it measures change in gross motor function, as rolling from supine position, sitting, walking, running, and jumping, among others, in children with cerebral palsy), and the sitting postural control.[32,37]

When NMES was used for the upper limbs, improvements were observed in the functional upper limb test,[35] the hand behind head test,[36] hand to mouth test,[36] tests of wrist abduction,[36] hand to back test,[36] and in the Melbourne Test,[33] although values returned to initial levels after the second month of follow-up without NMES. On the other hand, Yıldızgören et al[41] found no significant improvements in the hand ability test for children.

Regarding the use of NMES for the lower limbs, 6 studies[34,38,43,44,47,48] found improvements in the lower limb functional mobility tests. Of these studies, one[34] found significant improvements in the selective control assessment of the lower limb, whereas another[38] found significant improvements in the standing and walking items of the GMFM, and

Table 1. Risk-of-Bias Assessment

Study	Randomization Process[a]	Deviations from Intended Interventions[a]	Missing Outcome Data[a]	Measurement of the Outcome[a]	Selection of the Reported Result[a]	Total Score[a]	Risk of Bias
Elshazly (2001)[31]	−1	1	1	−1	0	0	High
Karabay et al (2016)[32]	0	1	1	−1	1	2	Some concerns
Ozer et al (2006)[33]	1	1	1	1	1	5	Low
Pool et al (2016)[34]	0	1	1	−1	1	2	Some concerns
Xu et al (2015)[35]	1	1	1	1	0	4	Low
Elnaggar (2016)[36]	1	1	1	1	1	5	Low
Elbasan et al (2018)[37]	1	0	1	1	1	4	Low
Chan et al (2004)[38]	0	−1	1	1	1	2	Some concerns
Fehlings et al (2002)[39]	1	1	1	−1	1	3	Some concerns
Karabay et al (2015)[40]	0	1	1	1	1	4	Low
Yildizgören et al (2014)[41]	−1	0	1	−1	−1	−2	High
Kang et al (2007)[42]	−1	0	1	−1	1	0	High
Arya et al (2012)[43]	0	1	1	1	1	4	Low
Sherief and Hamed (2013)[44]	1	0	1	1	1	4	Low
Detrembleur et al (2002)[45]	0	1	1	1	−1	2	Some concerns
Mudge et al (2015)[46]	0	−1	−1	−1	−1	−4	High
Qi et al (2018)[47]	1	1	1	1	1	5	Low
Kerr et al (2006)[48]	1	1	1	1	1	5	Low

[a] 1 = low; 0 = some concerns; −1 = high.

three[44,47,48] found significant improvements in the GMFM. However, Arya et al[43] showed no significant improvements.

A meta-analysis of GMFM data was performed to summarize the results of 9 groups from 6 studies. We found an overall statistically significant moderate effect of NMES compared with controls on the GMFM test (standardized mean difference = 0.41; 95% CI = 0.19-0.64), as depicted in Figure 2. Heterogeneity across studies was found to be relatively small and not statistically significant ($I^2 = 12.1\%$; χ^2 (8) = 9.10; $P = .334$). However, as the study by Qi et al[47] found a larger effect that was slightly out of funnel-plot 95% CI bounds (Suppl. Figure), the Egger test yielded a statistically significant bias coefficient ($P = .010$) that would not have reached significance if the study were excluded ($P = .271$).

In addition, 1 article assessed the functional mobility. Arya et al[43] obtained significant improvements in the physiological cost index of walking (ie, reduction in physiological cost indicating greater energy efficiency of walking).

Muscle Strength

For the upper limb (Tab. 4), 2 authors[33,35] found significant improvements in manual grip strength. Fehlings et al[39] showed no significant improvements for both manual muscle tests and the shoulder abductor quantitative myometry test.

On the other hand, all authors[34,38,48] found significant improvements for the lower limb strength tests. Improvements were found in the maximum extension torque of the knee in both the most and least affected leg,[48] the ankle dorsiflexion force,[34] the ankle dorsiflexion power ratio,[38] and the ratio of the dorsiflexion torque of the ankle,[38] in which values returned to initial levels after a follow-up period of 2 weeks without NMES.

Spasticity and Muscle Architecture

This category is presented together with the body composition (Tab. 5). Regarding spasticity, 1 author[31] found a significant reduction in the Hofman/myogenic ratio (ie, reduction of hypertonia), and another author[47] found a significant improvement on the Comprehensive Spasticity Scale.

As for muscle architecture, the effects on the anterior tibial muscle were positive in the length of the fascicle,[40] the cross-sectional area,[40] muscle volume,[34] and symmetry of the ratio.[34] The effects over the gastrocnemius were also positive in the phase angle,[40] cross-sectional area,[40] muscle volume,[34] and symmetry of the ratio.[34] In another study,[34] several areas of the lower limbs were also measured, showing both muscle volume and the symmetry of the ratio of muscle volume.[34] No representative increase was found for the soleus.[34]

Body Composition

This category is presented together with spasticity and muscle architecture (Tab. 5). In the study by Elnaggar,[36] bone mineral density was measured, through dual-energy x-ray absorptiometry, and significant improvements were found.

Discussion

After reviewing the 18 articles included in this systematic review and performing statistical analysis for the GMFM, we found that the use of NMES programs for children diagnosed with cerebral palsy, spinal muscular atrophy, and obstetric

Table 2. Biomechanics of Movement[a]

Study	Design	Group Data	Type of Cerebral Palsy (No. of Children)	Instrument(s)	NMES Protocol		Intervention	Results	Comparison of Changes for CG vs AG
					Body Part	Parameters			
Elshazly (2001)[31]	No RCT NMES + CG	22 children (14 M, 8 F) CG: 11 (5–9 y old) AG: 11 (5–9 y old)	Left hemiplegia (9) Right hemiplegia (12)		Tibia (LowL)	Dual-channel battery Frequency: 35–45 Hz Intensity: <10 mA Pulse width: 300 μs	Type: physical therapy Frequency: 60 min 6 d/wk Duration: 12 wk Supervised: semi Place: home	Step length ↑ Step width ↑ Foot angle ↑	SMD = 0.41; 95% CI = −0.40 to 1.23 SMD = 0.70; 95% CI = −0.13 to 1.53 SMD = 0.52; 95% CI = −0.30 to 1.34
Karabay et al (2016)[32]	RCT NMES + KT + CG	61 children (33 M, 28 F) CG: 19 (8 F) (5.7 [SD = 2.4] y old) KT group: 19 (9 F) (6.5 [SD = 2.4] y old) NMES group: 23 (11 F) (5.9 [SD = 2] y old)	Spastic diplegia	MAS (score)	Back (trunk)	2-channel, multimodal Frequency: 25 Hz Duration: on 10 s, off 12 s Intensity: 20–30 mA Pulse width: 250 μs	Type: physical therapy Frequency: 75 min 4 d/wk Duration: 4 wk Supervised: yes Place: rehabilitation center	Kyphosis angle ↑	SMD = −1.74; 95% CI = −2.44 to −1.04
Pool et al (2016)[34]	RCT Botox Botox-NMES	32 children (17 M, 15 F) CG: 16 (8 F) (10.4 [SD = 2.67] y old) AG: 16 (7 F) (10.9 [SD = 2.83] y old)	Unilateral spasticity	GMFCS	Ankle (LowL)	Asymmetrical biphasic surface electrical Frequency: 33 Hz Pulse width: 100 μs	Type: exercise and occupational therapy Frequency: 4 h 6 d/wk Duration: 8 wk of treatment, 6 wk of follow-up Supervised: no Place: home	SMC ↑	SMD = 0.79; 95% CI = 0.09 to 1.49
Yıldızgören et al (2014)[41]	RCT NMES + CG	24 children (14 M, 10 F) CG: 12 (5 F) (7.4 [SD = 2.6] y old) AG: 12 (5 F) (8.2 [SD = 2.2] y old)	Wrist and finger flexor spasticity	ZS MAS (score) GON	Arm (UpL)	Dual-channel Duration: 12 s on, 5 s off Frequency: 30 Hz Intensity: 10–25 mA Pulse width: 300 μs	Type: rehabilitation program Frequency: 30 min 5 d/wk Duration: 6 wk Supervised: no Place: home	WEA ↑	SMD = 1.08; 95% CI = 0.25 to 1.91

(*Continued*)

Table 2. Continued

Study	Design	Group Data	Type of Cerebral Palsy (No. of Children)	Instrument(s)	NMES Protocol		Intervention	Results	Comparison of Changes for CG vs AG
					Body Part	Parameters			
Kang et al (2007)[42]	No RCT NMES-BOTOX + BOTOX	18 children (9 M, 9 F) CG: 11 (3.75 y old) (1–10 y old) AG: 7 (3.75 y old) (1–10 y old)		MAS (score) GON	Equinus foot and hind foot (LowL)	2-channel device Frequency: 40 Hz Duration: 0.3 μs	Type: physical therapy Frequency: 30 min 2 d/wk Duration: 12 wk Supervised: yes Place: home	Popliteal angle ↔ Ankle dorsiflexion ↑ Equinus foot ↑ Hind foot ↔ Genu recurvatum ↔ Speed gait ↔ Crouch gait ↑	SMD = −0.43; 95% CI = −1.34 to 0.48 SMD = 0.27; 95% CI = −0.64 to 1.17 SMD = 1.02; 95% CI = 0.06 to 1.98 SMD = −0.23; 95% CI = −1.13 to 0.68 SMD = 0.49; 95% CI = −0.42 to 1.40 SMD = 0.15; 95% CI = −0.75 to 1.05 SMD = 0.49; 95% CI = −0.43 to 1.40
Arya et al (2012)[43]	RCT NMES + CG	10 children (5 M, 5 F) CG: 5 (3 F) (9.25 [SD = 2.98] y old) AG: 5 (2 F) (8.75 [SD = 2.21] y old)	Hemiplegia and diplegia	MAS (score)	Quadriceps and tibia (LowL)	Multichannel neuromuscular stimulator Frequency: 20–40 Hz Duration: 3 s on, 14 s off	Type: NMES Frequency: 20–30 min 4 or 5 d/wk Duration: 4 wk Supervised: yes Place: N/R	Cadence (steps/min) ↑ Step length (cm) ↔ Speed (m/min) ↑	SMD = 1.06; 95% CI = −0.14 to 2.26 SMD = 0.01; 95% CI = −1.09 to 1.12 SMD = 1.34; 95% CI = 0.09 to 2.60
Sherief and Hamed (2013)[44]	RCT Exercise-NMES (CG) + trampoline (AG)	30 children (12 M, 18 F) (5–8 y old) CG: 15 AG: 15	Central hypotonia	GON Radiograph	Leg (LowL)	N/R Frequency: N/R Pulse width: N/R	Type: rebound therapy Frequency: 30 min 5 d/wk Duration: 12 wk Supervised: yes Place: N/R	GRA ↑ KHR ↑	SMD = 0.00; 95% CI = −0.70 to 0.70 SMD = −0.04; 95% CI = −0.74 to 0.65

(*Continued*)

Table 2. Continued

Study	Design	Group Data	Type of Cerebral Palsy (No. of Children)	Instrument(s)	NMES Protocol		Intervention	Results	Comparison of Changes for CG vs AG
					Body Part	Parameters			
Detrembleur et al (2002)[45]	RCT BOTOX + Botox-NMES	12 children (8 M, 4 F) Median age = 5 y (4.8–6 y old) CG: 6 AG: 6	Hemiplegia (9) Diplegia (3)	MAS (score)	Leg (LowL)	2-channel device Frequency: 20 Hz Intensity: 50–90 mA Pulse width: 200 μs	Type: physical therapy Frequency: 30 min 6 d/wk Duration: 24 wk Supervised: yes Place: N/R	ROM ↔ VS ↑ APF ↑ PAW ↑ NAW ↑ CF ↑ CD ↑ PRS ↑ Equinus foot ↑ Step length (m) ↔ Cadence (steps/min) ↔ Speed (km/h) ↔ AFMS ↑ PL ↑ AD ↑	N/R N/R N/R N/R N/R N/R N/R N/R N/R N/R N/R N/R N/R N/R N/R
Mudge et al (2015)[46]	RCT Counter leg (CG) Botox + NMES-Botox	6 children (3 M, 3 F) (9.1 y old) (8.7–9.2 y old)	Spastic diplegia	GMFM GON INCL	Leg (LowL)	N/R Frequency: 50 Hz Pulse width: 260 μs	Type: stretching Frequency: 30 min 5 d/wk Duration: 12 wk Supervised: yes Place: rehabilitation center	PAI ↔ PAG ↔	SMD = −0.13; 95% CI = −1.17 to 0.90 SMD = 0.00; 95% CI = −1.04 to 1.04
Qi et al (2018)[47]	RCT NMES + NMES-exercise	100 children (53 M, 47 F) CG: 50 (23 F) (6 [SD = 2.8] y old) AG: 50 (24 F) (5.8 [SD = 2.9] y old)		CSS	Leg (LowL)	N/R Duration: 20 min Frequency: N/R Intensity: just enough to cause muscle contraction	Type: strength training Frequency: 30 min 5 d/wk Duration: 12 wk (3 wk of follow-up) Supervised: yes	WS (m/s) ↑ (3 wk of follow-up) ↔	SMD = 0.95; 95% CI = 0.54 to 1.36

[a] AD = ankle dorsiflexion; AFMS = ankle flexor muscle stiffness; AG = active group; APF = ankle plantarflexion; Botox = Botulinum toxin; CD = cocontraction dorsiflexion; CF = cocontraction flexion; CG = control group; CSS = Comprehensive Spasticity Scale; F = female; GMFCS = Gross Motor Function Classification System; GMFM = Gross Motor Function Measure; GON = goniometer; GRA = genu recurvatum angle; INCL = inclinometer; KHR = knee hyperextension range; KT = Kinesio Taping; LowL = lower limb; M = male; MAS = Modified Ashworth Scale; NAW = negative ankle work; NMES = neuromuscular electrical stimulation; N/R = not reported; PAG = popliteal angle goniometer; PAI = popliteal angle inclinometer; PAW = positive ankle work; PL = path length; PRS = Physician Rating Scale; RCT = randomized controlled trial; ROM = range of motion; SMC = selective motor control; SMD = standardized mean difference; UpL = upper limb; VS = viscous stiffness; WEA = wrist extension angle; WS = walking speed; ZS = Zancolli Scale; ↑ = increased; ↔ = unchanged.

Table 3. Functional Mobility[a]

Study	Design	Group Data	Disease (No. of Children)	Instruments	NMES protocol		Intervention	Results	Comparison of Change CG vs AG
					Body Part	Parameters			
Karabay et al (2016)[32]	RCT NMES + KT + CG	61 children (33 M, 28 F) CG: 19 (8 F) (5.7 [SD = 2.4] y old) KT group: 19 (9 F) (6.5 [SD = 2.4] y old) NMES group: 23 (11 F) (5.9 [SD = 2] y old)	Cerebral palsy with spastic diplegia	MAS (score)	Back (trunk)	2-channel, multimodal Frequency: 25 Hz Duration: 10 s on, 12 s off Intensity: 20–30 mA Pulse width: 250 μs	Type: physical therapy Frequency: 75 min 4 d/wk Duration: 4 wk Supervised: yes Place: rehabilitation center	GMFM ↑	SMD = 0.50; 95% CI = −0.10 to 1.11
Ozer et al (2006)[33]	Prospective RCT NMES + NMES-DB + DB	24 children (12 M, 12 F) DB group: 8 (5 F) (8.8 y old) NMES-DB group: 8 (3 F) (7.3 y old) NMES group: 8 (4 F) (9.7 y old)	Cerebral palsy Spastic right (13) Spastic left (11)	ZS	Arm (UpL)	Dual-channel battery-powered Duration: 60 pulses/s, 10 s on, 7 s off Intensity: 30–40 mA Pulse width: 200 μs	Type: mobilization (DB) + NMES Frequency: 60 min 7 d/wk Duration: 24 wk of training and 12 wk of follow-up Supervised: no Place: home	Melbourne Test ↑ Decreased after the second month	SMD = 0.25; 95% CI = −0.68 to 1.17
Pool et al (2016)[34]	RCT Botox + Botox-NMES	32 children (17 M, 15 F) CG: 16 (8 F) (10.4 [SD = 2.67] y old) AG: 16 (7 F) (10.9 [SD = 2.83] y old)	Cerebral palsy with unilateral spasticity	GMFCS	Ankle (LowL)	Asymmetrical biphasic surface electrical Frequency: 33 Hz Pulse width: 100 μs	Type: exercise and occupational therapy Frequency: 4 h 6 d/wk Duration: 8 wk of treatment, 6 wk of follow-up Supervised: no Place: home	SCALE ↑	SMD = 0.31; 95% CI = −0.37 to 0.99
Xu et al (2015)[35]	RCT NMES-CT + CT + CG	46 children (18 M, 28 F) CG: 23 (12 F) (4.6 [SD = 2.57] y old) NMES-CT group: 23 (16 F) (4.7 [SD = 2.83] y old)	Cerebral palsy with hemiplegia	GMFCS	Arm (UpL)	Dual-channel Duration: 12 s on, 12 s off Frequency: 50 Hz Intensity: 100 mA Pulse width: 300 μs	Type: functional therapeutic activities and occupational therapy Frequency: 2 h 7 d/wk Duration: 24 wk Supervised: no Place: home/hospital	UEFT ↑	N/R
Elnaggar (2016)[36]	RCT Therapy + therapy-NMES	42 children (16 M, 26 F) CG: 21 (12 F) (4.05 [SD = 0.8] y old) AG: 21 (14 F) (3.67 [SD = 0.73] y old)	Obstetric brachial plexus injury		Arm (UpL)	Faradic stimulator Duration: 15 s on, 15 s off Frequency: 30 Hz Pulse width: 300 μs	Type: physical therapy program Frequency: 40 min 7 d/wk Duration: 12 wk Supervised: no Place: home	Abduction ↑ External rotation ↑ Hand behind head ↑ Hand to back ↑ Hand to mouth ↑	SMD = 0.30; 95% CI = −0.30 to 0.89 SMD = −0.67; 95% CI = −1.28 to −0.06 SMD = 1.31; 95% CI = 0.65 to 1.97 SMD = 0.23; 95% CI = −0.36 to 0.83 SMD = 0.43; 95% CI = −0.17 to 1.03

(*Continued*)

Table 3. Continued

Study	Design	Group Data	Disease (No. of Children)	Instruments	NMES protocol		Intervention	Results	Comparison of Change CG vs AG
					Body Part	Parameters			
Elbasan et al (2018)[37]	Cross-sectional study NDT + NDT-NMES + NDT-NMES-KT	45 children (22 M, 23 F) CG: 15 (7 F) (7.8 [SD = 2.61] y old) NMES group: 15 (8 F) (6.8 [SD = 2.11] y old) NMES-KT group: 15 (8 F) (9.1 [SD = 2.91] y old)	Cerebral palsy Spastic diplegia (9) Quadriplegia (36)	GMFCS	Paravertebral (trunk)	Current with double peak as type of pulse Duration: 14.65 ms Frequency: 60 Hz	Type: NDT Frequency: 15 min 4 d/wk Duration: 6 wk Supervised: semi Place: physical therapy center	GMFM ↑ SPCM ↑	SMD = 0.16; 95% CI = −0.54 to 0.86 SMD = 0.40; 95% CI = −0.30 to 1.11
Chan et al (2004)[38]	RCT NMES-exercise + exercise (CG)	12 children (9 M, 3 F) CG: 6 (2 F) (6.3 [SD = 1.03] y old) AG: 6 (1 F) (6.5 [SD = 2.74] y old)	Cerebral palsy Diplegia (7) Hemiplegia (5)	MAS (score)	Triceps surae (LowL)	Portable NMES with remote control leads Frequency: 30–35 pulses/s Intensity: until visible muscle contraction was reached	Type: cardiovascular Frequency: 15 min 3 d/wk Duration: 8 wk Supervised: yes Place: N/R	GMST ↑ GMWK ↑	SMD = 0.14; 95% CI = −0.89 to 1.18 SMD = 0.03; 95% CI = −1.00 to 1.07
Yıldızgören et al (2014)[41]	RCT NMES + CG	24 children (14 M, 10 F) CG: 12 (5 F) (7.4 [SD = 2.6] y old) AG: 12 (5 F) (8.2 [SD = 2.2] y old)	Cerebral palsy with wrist and finger flexor spasticity	ZS MAS (score)	Arm (UpL)	Dual-channel Duration: 12 s on, 5 s off Frequency: 30 Hz Intensity: 10–25 mA Pulse width: 300 μs	Type: rehabilitation program Frequency: 30 min 5 d/wk Duration: 6 wk Supervised: no Place: home	Abilhand-Kids Test ↔	SMD = 1.16; 95% CI = 0.33 to 2.00
Arya et al (2012)[43]	RCT NMES + CG	10 children (5 M, 5 F) CG: 5 (3 F) (9.25 [SD = 2.98] y old) AG: 5 (2 F) (8.75 [SD = 2.21] y old)	Cerebral palsy with hemiplegia and diplegia	MAS (score)	Quadriceps and tibia (LowL)	Multichannel neuromuscular stimulator Frequency: 3 s on, 14 s off; 5 s of relaxation; 20–40 Hz	Type: NMES Frequency: 20–30 min 4 or 5 d/wk Duration: 4 wk Supervised: yes Place: N/R	GMFM ↔ PCI ↑	SMD = 0.02; 95% CI = −1.09 to 1.12 SMD = −2.59; 95% CI = −4.17 to −1.00

(*Continued*)

Table 3. Continued

Study	Design	Group Data	Disease (No. of Children)	Instruments	NMES protocol		Intervention	Results	Comparison of Change CG vs AG
					Body Part	Parameters			
Sherief and Hamed (2013)[44]	RCT Exercise -NMES (CG) + trampoline (AG)	30 children (12 M, 18 F) (5–8 y old) CG: 15 AG: 15	Cerebral palsy with central hypotonia		Leg (LowL)	N/R Frequency: N/R Pulse width: N/R	Type: rebound therapy Frequency: 30 min 5 d/wk Duration: 12 wk Supervised: yes Place: N/R	GMFM ↑	SMD = 0.25; 95% CI = −0.45 to 0.94
Qi et al (2018)[47]	RCT NMES + NMES-exercise	100 children (53 M, 47 F) CG: 50 (23 F) (6 [SD = 2.8] y old) AG: 50 (24 F) (5.8 [SD = 2.9] y old)	Cerebral palsy	CSS	Leg (LowL)	N/R Duration: 20 min Frequency: N/R Intensity: just enough to cause muscle contraction	Type: strength training Frequency: 30 min 5 d/wk Duration: 12 wk (3 wk follow-up) Supervised: yes Place: N/R	GMFM ↑	SMD = 0.95; 95% CI = 0.54 to 1.37
Kerr et al (2006)[48]	RCT NMES + TENS + CG	60 children (38 M, 22 F) CG: 22 (7 F) (10.6 [SD = 3.91] y old) TENS group: 20 (9 F) (11.5 [SD = 3.15] y old) NMES group: 18 (6 F) (11.1 [SD = 3.43] y old)	Cerebral palsy Diplegia (55) Quadriplegia (1) Dystonia (1) Ataxia (1) Nonclassifiable (2)	LAS	Leg (LowL)	N/R Duration: 7 s on, 2 s off Frequency: 35 Hz Intensity: maximum tolerable Pulse width: 300 μs	Type: NMES Frequency: 1 h of NMES; TENS, and CG for 8 h 5 d/wk Duration: 14 wk Supervised: semi Place: home	GMFM ↑	SMD = 0.21; 95% CI = −0.40 to 0.82

[a]AG = active group; Botox = Botulinum toxin; CG = control group; CSS = Comprehensive Spasticity Scale; CT = constraint therapy; DB = dynamic bracing; F = female; GMFCS = Gross Motor Function Classification System; GMFM = Gross Motor Function Measure; GMST = Gross Motor Standing Test; GMWK = Gross Motor Walking Test; KT = Kinesio Taping; LAS = Lifestyle Assessment Score; LowL = lower limb; M = male; MAS = Modified Ashworth Scale; NDT = neurodevelopmental treatment; NMES = neuromuscular electrical stimulation; N/R = not reported; PCI = physiological cost index; RCT = randomized controlled trial; SCALE = selective control assessment of the lower limb; SMD = standardized mean difference; SPCM = seated postural control measurement; TENS = transcutaneous electrical nerve stimulation; UEFT = upper extremity functional test; UpL = upper member; ZS = Zancolli Scale; ↑ = increased; ↔ = unchanged.

Table 4. Muscle Strength[a]

Study	Design	Group Data	Disease (No. of Children)	Instrument(s)	NMES Protocol		Intervention	Results	Comparison of Changes for CG vs AG
					Body Part	Parameters			
Ozer et al (2006)[33]	Prospective RCT NMES + NMES-DB + DB	24 children (12 M, 12 F) DB group: 8 (5 F) (8.8 y old) NMES-DB group: 8 (3 F) (7.3 y old) NMES group: 8 (4 F) (9.7 y old)	Cerebral palsy Spastic right (13) Spastic left (11)	Standard dynamometer ZS	Arm (UpL)	Dual-channel battery-powered Duration: 60 pulses/s; 10 s on, 7 s off Intensity: 30-40 mA Pulse width: 200 μs	Type: mobilization (DB) + NMES Frequency: 60 min 7 d/wk Duration: 24 wk of training and 12-wk follow-up Supervised: no Place: home	Grip strength (%) ↑ Decreased after 2 mo from end of study, returning to normal values	SMD = 0.55; 95% CI = −0.39 to 1.50
Pool et al (2016)[34]	RCT Botox + Botox-NMES	32 children (17 M, 15 F) CG: 16 (8 F) (10.4 [SD = 2.67] y old) AG: 16 (7 F) (10.9 [SD = 2.83] y old)	Cerebral palsy with unilateral spasticity	GMFCS	Ankle (LowL)	Asymmetrical biphasic surface electrical Frequency: 33 Hz Pulse width: 100 μs	Type: exercise and occupational therapy Frequency: 4 h 6 d/wk Duration: 8 wk of treatment, 6 wk follow-up Supervised: no Place: home	Dorsiflexion ↑(normalized)	SMD = 0.92; 95% CI = 0.21 to 1.63
Xu et al (2015)[35]	RCT NMES-CT + CT + CG	46 children (18 M, 28 F) CG: 23 (12 F) (4.6 [SD = 2.57] y old) NMES-CT group: 23 (16 F) (4.7 [SD = 2.83] y old)	Cerebral palsy with hemiplegia	GMFCS SPHY	Arm (UpL)	Dual-channel Duration: 12 s on, 12 s off Frequency: 50 Hz Intensity: 100 mA Pulse width: 300 μs	Type: functional and occupational therapy Frequency: 2 h 7 d/wk Duration: 24 wk Supervised: no Place: home/hospital	Hand grip strength ↑	N/R
Chan et al (2004)[38]	RCT NMES-exercise + exercise (CG)	12 children (9 M, 3 F) CG: 6 (2 F) (6.3 [SD = 1.03] y old) AG: 6 (1 F) (6.5 [SD = 2.74] y old)	Cerebral palsy Diplegia (7) Hemiplegia (5)	MAS (score)	Triceps surae (LowL)	Portable NMES with remote control leads Duration: 30–35 pulses/s Intensity: until visible muscle contraction was reached	Type: cardiovascular Frequency: 15 min 3 d/wk Duration: 8 wk Supervised: yes Place: N/R	APQ ↑ AMQ ↑	SMD = −1.28; 95% CI = −2.44 to −0.12 SMD = −0.51; 95% CI = −1.57 to 0.55

(*Continued*)

Table 4. Continued

Study	Design	Group Data	Disease (No. of Children)	Instrument(s)	NMES Protocol		Intervention	Results	Comparison of Changes for CG vs AG
					Body Part	Parameters			
Fehlings et al (2002)[39]	RCT NMES + opposite arm (CG)	13 children (10 M, 3 F) AG-CG: 13 (3 F) (9.9 [SD = 3.36] y old)	Spinal muscular atrophy Level II (7) Level III (6)	QMT	Arm (UpL)	Dual-channel battery Frequency: 35–45 Hz Intensity: <10 mA Pulse width: 300 μs	Type: night stimulation Frequency: 4 h 7 d/wk Duration: 48 wk of treatment, 24 wk of control Supervised: no Place: home	QMT abductors ↑ QMT flexors ↑ MMT abductors ↑ MMT flexors ↑	SMD = 0.19; 95% CI = −0.56 to 0.93 SMD = 0.37; 95% CI = −0.38 to 1.12 SMD = 0.17; 95% CI = −0.57 to 0.92 SMD = 0.05; 95% CI = −0.69 to 0.79
Kerr et al (2006)[48]	RCT NMES + TENS + CG	60 children (38 M, 22 F) CG: 22 (7 F) (10.6 [SD = 3.91] y old) TENS group: 20 (9 F) (11.5 [SD = 3.15] y old) NMES group: 18 (6 F) (11.1 [SD = 3.43] y old)	Cerebral palsy	Isokinetic dynamometer LAS	Leg (LowL)	N/R Duration: 7 s on, 12 s off, increased the intensity Frequency: 35 Hz Intensity: maximum tolerable Pulse width: 300 μs	Type: NMES Frequency: 1 h of NMES; TENS and CG for 8 h 5 d/wk Duration: 14 wk Supervised: semi Place: home	PTMAL (N·m) ↑ PTLAL (N·m) ↑	SMD = 0.33; 95% CI = −0.29 to 0.94 SMD = 0.32; 95% CI = −0.29 to 0.94

[a] AG = active group; AMQ = ankle moment quotient; APQ = ankle power quotient; Botox = Botulinum toxin; CG = control group; CT = constraint therapy; DB = dynamic bracing; F = female; GMFCS = Gross Motor Function Classification System; LAS = Lifestyle Assessment Score; LowL = lower member; M = male; MAS = Modified Ashworth Scale; MMT = manual muscle testing; NMES = neuromuscular electrical stimulation; N/R = not reported; PTLAL = peak torque of least affected leg; PTMAL = peak torque of most affected leg; QMT = quantitative myometer testing; RCT = randomized controlled trial; SMD = standardized mean difference; SPHY = sphygmomanometer; TENS = transcutaneous electrical nerve stimulation; UpL = upper member; ZS = Zancolli Scale; ↑ = increased.

Table 5. Spasticity, Muscle Architecture, and Body Composition[a]

Parameter	Study	Design	Group Data	Disease (No. of Children)	Instruments	NMES Protocol		Intervention	Results	Comparison of Changes for CG vs AG
						Body Part	Parameters			
Spasticity	Elshazly (2001)[31]	No RCT NMES + CG	22 children (14 M, 8 F) CG: 11 (5–9 y old) AG: 11 (5–9 y old)	Cerebral palsy Left hemiplegia (9) Right hemiplegia (11)		Tibia (LowL)	Dual-channel battery Frequency: 35–45 Hz Intensity: <10 mA Pulse width: 300 μs	Type: physical therapy Frequency: 60 min 6 d/wk Duration: 12 wk Supervised: semi Place: home	H/M (ratio) ↓	SMD = −0.45; 95% CI = −1.27 to 0.36
	Qi et al (2018)[47]	RCT NMES + NMES-exercise	100 children (53 M, 47 F) CG: 50 (23 F) (6 [SD = 2.8] y old) AG: 50 (24 F) (5.8 [SD = 2.9] y old)	Cerebral palsy	CSS	Leg (LowL)	N/R Duration: 20 min Frequency: N/R Intensity: just enough to cause muscle contraction	Type: strength training Frequency: 30 min 5 d/wk Duration: 12 wk (3-wk follow-up) Supervised: yes Place: N/R	CSS ↑	SMD = −0.49; 95% CI = −0.88 to −0.09
Muscle architecture	Pool et al (2016)[34]	RCT Botox + Botox-NMES	32 children (17 M, 15 F) CG: 16 (8 F) (10.4 [SD = 2.67] y old) AG: 16 (7 F) (10.9 [SD = 2.83] y old)	Cerebral palsy with unilateral spasticity	GMFCS	Ankle (LowL)	Asymmetrical biphasic surface electrical Frequency: 33 Hz Pulse width: 100 μs	Type: exercise and occupational therapy Frequency: 4 h 6 d/wk Duration: 8 wk of treatment, 6-wk follow-up Supervised: no Place: home	MV: TA ↑ MGC ↑ LGC ↑ Sol ↔ MVSR: TA ↑ MGC ↑ LGC ↑ Sol ↔	SMD = 0.50; 95% CI = −0.19 to 1.18 SMD = 0.22; 95% CI = −0.45 to 0.90 SMD = 0.32; 95% CI = −0.36 to 1.00 SMD = −0.02; 95% CI = −0.70 to 0.65 SMD = 0.55; 95% CI = −0.14 to 1.24 SMD = 0.35; 95% CI = −0.33 to 1.03 SMD = 0.40; 95% CI = −0.28 to 1.08 SMD = −0.12; 95% CI = −0.80 to 0.56

(*Continued*)

Table 5. Continued

Parameter	Study	Design	Group Data	Disease (No. of Children)	Instruments	NMES Protocol		Intervention	Results	Comparison of Changes for CG vs AG
						Body Part	Parameters			
	Karabay et al (2015)[40]	RCT NMES + CG Counter leg (control)	28 children (17 M, 11 F) CG: 14 (4 F) (6.3 [SD = 2.42] y old) AG: 14 (7 F) (7.2 [SD = 1.91] y old)	Cerebral palsy with spastic diplegia	MAS SMC	Leg (LowL)	2-channel, multimodal Frequency: 25 Hz Duration: 10 s on, 12 s off Intensity: 20-30 mA Pulse width: 250 μs	Type: physical therapy Frequency: 30 min 5 d/wk Duration: 4 wk Supervised: yes Place: rehabilitation center	TA muscle CSA (mm^2) ↑ PA (°) ↔ FL (mm) ↔ GC muscle CSA (mm^2) ↑ PA (°) ↔ FL (mm) ↔	SMD = 0.93; 95% CI = 0.17 to 1.69 SMD = −0.07; 95% CI = −0.79 to 0.65 SMD = −0.38; 95% CI = −1.10 to 0.35 SMD = 0.55; 95% CI = −0.18 to 1.29 SMD = 0.22; 95% CI = −0.50 to 0.94 SMD = −0.08; 95% CI = −0.80 to 0.64
Body composition	Elnaggar (2016)[36]	RCT Therapy + therapy-NMES	42 children (16 M, 26 F) CG: 21 (12 F) (4.05 [SD = 0.8] y old] AG: 21 (14 F) (3.67 [SD = 0.73] y old)	Obstetric brachial plexus injury	DEXA	Arm (UpL)	Faradic stimulator Duration: 15 s on, 15 s off Frequency: 30 Hz Pulse width: 300 μs	Type: physical therapy program Frequency: 40 min 7 d/wk Duration: 12 wk Supervised: no Place: home	BMD ↑	SMD = 0.47; 95% CI = −0.13 to 1.07

[a] AG = active group; BMD = bone mineral density; Botox = Botulinum toxin; CG = control group; CSA = cross-sectional area; CSS = Comprehensive Spasticity Scale; DEXA = dual-energy x-ray absorptiometry; F = female; FL = fascicle length; GC = gastrocnemius; GMFCS = Gross Motor Function Classification System; H/M = Hofman/myogenic; LGC = lateral gastrocnemius; LowL = lower member; M = male; MAS = Modified Ashworth Scale; MGC = medial gastrocnemius; MV = muscle volume; MVSR = muscle volume symmetry ratio; NMES = neuromuscular electrical stimulation; N/R = not reported; PA = pennation angle; RCT = randomized controlled trial; SMC = selective motor control; SMD = standardized mean difference; Sol = soleus; TA = tibial anterior; UpL = upper member; ↓ = decreased; ↑ = increased; ↔ = unchanged.

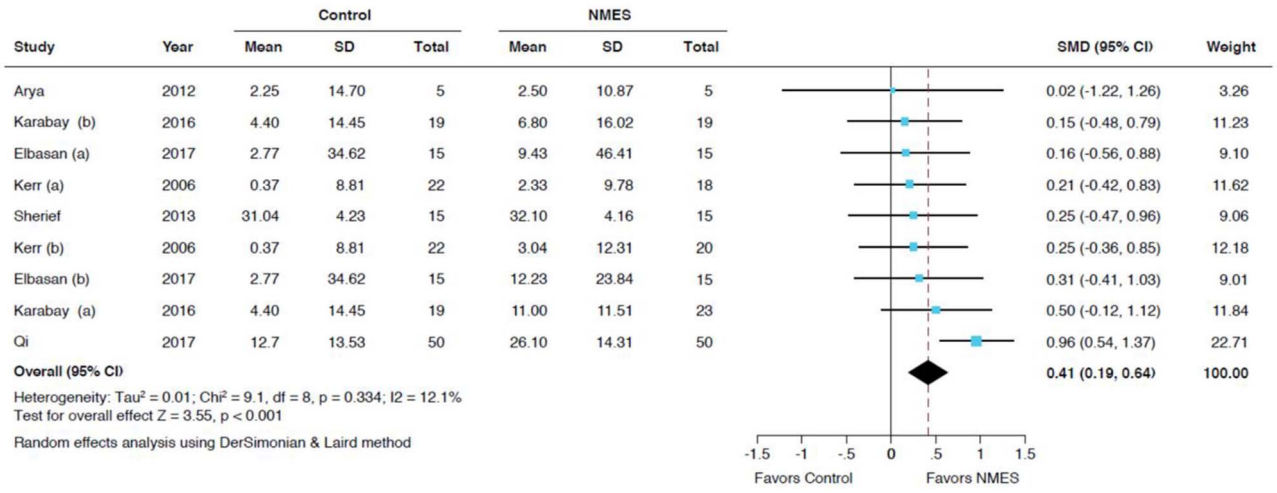

Figure 2. Forest plot of neuromuscular electrical stimulation (NMES) effects on Gross Motor Functional Measure (GMFM) compared with control.

injury of the brachial plexus seems to be effective in improving strength, biomechanics of movement, and functional mobility.However, to date, there are not enough studies to confirm that NMES produces benefits on spasticity, muscle architecture, and body composition.

Biomechanics of Movement

The results evaluated show that an NMES program has positive effects on the ROM of the spine[32] and the wrist,[41] although only a positive trend was found for the lower limbs. Three studies[31,42,45] found a positive effect on some of the variables measured on the ankle and knee ROM, whereas 1 author[46] did not observe changes in these variables. The results for the wrist are in agreement with the study by Kamper et al,[49] in patients with cerebral palsy, where a 38 degree improvement in the ROM was reported after an NMES program.

Regarding gait biomechanical variables, significant improvements in walking speed after a program of NMES were observed.[43,47] These results are in agreement with both the study by Chiu and Ada[50] and that of Stackhouse et al,[14] because both conclude that although exercise programs present better results, NMES can be very effective in improving walking speed in patients who are not able to perform an exercise program. In contrast, 2 studies did not report improvements,[42,45] agreeing with the systematic review by Moll et al,[51] in which the walking speed was negatively altered by the use of NMES. These discrepancies may be associated with the application of NMES in a nonspecific muscular area, which would not play an important role in walking. Moreover, walking speed is a predictive marker related to the number of hospitalizations and life expectancy.[52] Then, the improvements reported in walking speed may go further than better gait biomechanics, and might have a positive impact on the patient's health and longevity.

Other variables analyzed were the crouch gait, path length, and length and width of the step. The crouch gait is characteristic of patients with cerebral palsy, where a significant increase in speed was observed in the only study analyzing it.[42] With respect to the other variables, 2 studies[31,43] showed an improvement in path length, and in both, length and width of the step, and in one in the global score of the Physician Rating Scale.[45] These data coincide with the review by Mooney and Rose,[53] in which they report an improvement in the length of the step, and also with an improvement in the biomechanics of gait observed by Pool et al[54]—both cases in children with cerebral palsy. Conversely, 2 other authors[43,45] did not obtain changes in these same variables, coinciding with the review by Khamis et al,[55] in which insufficient evidence for correcting the alterations of the gait pattern was found.

Functional Mobility

Regarding the functional mobility tests, we observed that the majority of the analyzed articles presented improvements following an NMES program,[32–35,37,38,43,45,47,48] and only 2 studies did not confirm these effects.[41,43] Functional mobility tests are performed with the objective of evaluating the patient's body functionality both globally and by segments. One of the most relevant and widely used tests is the GMFM,[56] for which 4 authors have shown improvements[37,41,42,44] and only 1 did not,[43] which could be related to the limited sample size of the study. The results of the present meta-analysis have shown a moderate effect size (ES), indicating that NMES seems to be an effective tool to improve gross motor function (GMFM test) in children, a result also supported by a previous meta-analysis.[20] Other variables of global body functionality where improvements were obtained are the physiological cost index.[43]

Regarding functional mobility by body segments, improvements for the trunk[37] (sitting postural control test), upper limbs[33,35] (ie, Melbourne Test and functional upper limb test), and lower limbs[46,57] (stand-up test and walk test) were found. However, 1 study[41] did not find significant improvements in the hand ability test for children, possibly due to the small sample size of the study.

Muscle Strength

Two studies found significant improvements in the strength of the upper limbs, as measured by manual dynamometry.[33,35] Indeed, Kamper et al[49] concluded that an NMES program improves the strength levels of the extensor muscles of the wrist and, consequently, the functionality of children with cerebral palsy. Conversely, another study[39] did not report improvements either in manual muscle tests, or in quantitative

myometry tests. However, for the strength of the lower limbs, all authors[34,38,48] showed significant improvements for the tests used, including the maximum knee extension torque of the most and least affected leg,[48] the dorsiflexion force of the ankle,[34,39] the power quotient and the ratio of the dorsiflexion torque of the ankle,[38] as well as the plantarflexion force.[39] These results are in agreement with both a systematic review[53] and the study by Stackhouse et al,[14] where a positive trend for the improvement of dorsiflexion of the ankle, and improvements for the strength levels of the femoral quadriceps and the triceps surae were observed in children with cerebral palsy.

Spasticity and Muscle Architecture

Regarding spasticity, 2 studies[31,47] found a significant improvement in spasticity on the Hofman/myogenic ratio[31] and on the Comprehensive Spasticity Scale.[47] Furthermore, few studies have attempted to determine the effects of NMES on muscle architecture,[34,40] showing inconsistent data for some muscles of the lower limbs (tibialis anterior, gastrocnemius, soleus). Our findings coincide with the review carried out by Mooney and Rose,[53] where improvements in muscle architecture (ie, muscle volume) were found, but conclusions were limited by the low level of evidence.

It is important to highlight that, although there is little evidence, the results in all the studies performed to date are positive and, therefore, the use of NMES seems promising. Thus, more research is needed to confirm that NMES can improve spasticity and muscle architecture in pediatric patients with CNDs or chronic diseases.

Body Composition

Only 1 study has attempted to determine the effects of NMES on body composition,[36] and significant improvements were found in bone mineral density. However, more research is needed to confirm that NMES can improve body composition and specifically bone mineral density in children with CNDs or chronic diseases.

NMES Protocols

The NMES programs included in the studies analyzed in the present review have used frequencies of 20 to 35 Hz, agreeing with a previous systematic review[50] concluding that 30 Hz is the average frequency used. The intensity applied during NMES ranges between 20 and 100 mA, again coinciding with the findings of a previous review.[51] However, it seems that a relationship between a higher or lower dose of NMES and a greater improvement of the measured variables was not observed.[51] A very important factor to take into account when designing NMES programs is the execution time. Most of the NMES protocols found in the literature presented a duration of 6–8 weeks,[57] which is much shorter than the durations found in the present review, with an average of 14 weeks (ranging from 4 to 48 weeks). Most studies found that improvements are experienced after the first 2 weeks of the program.[20] In addition, several studies[39,48,49,58] have demonstrated the efficacy of NMES used alone. However, the use of NMES accompanied by other interventions, such as physical therapy,[36] occupational therapy,[35,43] and physical exercise,[15,34] have also proved efficient, because isolated use may sometimes be an insufficient stimulus to achieve relevant gains in the target variables related to the improvement of health and quality of life.[43,59]

Clinical Implications

NMES intervention programs in children with CNDs have shown to affect positively the strength, biomechanics of movement, upper and lower limb ROM, and functional mobility. Taking into account that cerebral palsy, obstetric brachial plexus injuries, and spinal muscular atrophy are very different conditions, our findings may be clinically relevant in demonstrating the improvement of common chronic symptoms in pediatric patients with these 3 diseases that affect daily activities and quality of life: (1) in cerebral palsy (eg, alterations in gait, postural control and balance, upper and lower limb ROM)[60]; (2) in spinal muscular atrophy (eg, skeletal muscle atrophy, alterations in gait, postural control and balance, upper and lower limb ROM)[61]; and (3) obstetric brachial plexus injuries (eg, numbness on the upper limbs; reduced ROM in shoulder and/or elbow, wrist, fingers; reduced strength on the upper limbs; and functional alterations in the activities of daily living performed with the upper limbs).[62]

We believe it is also important to highlight that, to the best of our knowledge, NMES was not used in other pediatric chronic diseases different from CNDs. The effects of NMES on muscle abilities (eg, strength, motor control, metabolism, and body composition), could help other patients cope with their symptoms and treatment side effects. Therefore, further research is required to assess how NMES may impact positively other chronic diseases in children (eg, obesity, diabetes, cancer, and respiratory and cardiovascular diseases).

Limitations

During the performance of this systematic review and meta-analysis, limitations were found, including the following, which we believe it is important to highlight: (1) There was little agreement in the variables analyzed in the different studies, which makes it difficult to compare the results and the statistical analysis of some variables. It would be advisable to attempt to unify assessment variables in the pediatric population with CNDs such as cerebral palsy, to allow for ES analysis and more precise comparisons, leading to the improved quality of conclusions. (2) There was a small sample size in most of the studies analyzed, which could be related to the difficulty in recruiting pediatric patients with CNDs. (3) The sample analyzed in the present study mostly comprised children with cerebral palsy, which makes it difficult to extrapolate conclusions to other CNDs or other chronic diseases with significant prevalence in children. (4) The modification of the final assessment of the RoB tool to adapt it to the non-RCT studies included in the present systematic review (ie, 2 non-RCTs, and 2 cross-sectional studies).

Conclusion

The use of NMES programs for pediatric patients with CNDs, specifically cerebral palsy, seems to be effective in improving muscle strength, and biomechanics of movement and functional mobility. However, benefits for spasticity, muscle architecture, and body composition are still not clear. RCTs focusing on analyzing the effects of NMES on spasticity, muscle architecture, and body composition in children with CNDs are still needed to allow for future effect size evaluation and effectiveness. Further research is also required to assess

the effects of NMES in pediatric patients with other chronic diseases.

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Systematic Review Registration

This protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO) (ref. no. CRD42020177651).

Disclosures

The authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

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