Neuromuscular electrical stimulation to augment lower limb exercise and mobility in individuals with spastic cerebral palsy: A scoping review

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Background: Neuromuscular Electrical Stimulation (NMES) is an emerging assistive technology applied through surface or implanted electrodes to augment skeletal muscle contraction. NMES has the potential to improve function while reducing the neuromuscular impairments of spastic cerebral palsy (CP). This scoping review examines the application of NMES to augment lower extremity exercises for individuals with spastic CP and reports the effects of NMES on neuromuscular impairments and function in spastic CP, to provide a foundation of knowledge to guide research and development of more effective treatment.

Methods: A literature review of Scopus, Medline, Embase, and CINAHL databases were searched from 2001 to 2 November 2021 with identified inclusion and exclusion criteria.

Results: Out of 168 publications identified, 33 articles were included. Articles on three NMES applications were identified, including NMES-assisted strengthening, NMES-assisted gait, and NMES for spasticity reduction. NMES-assisted strengthening included the use of therapeutic exercises and cycling. NMES-assisted gait included the use of NMES to improve gait patterns. NMES-spasticity reduction included the use of transcutaneous electrical stimulation or NMES to decrease tone. Thirteen studies investigated NMES-assisted strengthening, eleven investigated therapeutic exercise and demonstrated significant improvements in muscle structure, strength, gross motor skills, walking speed, and functional mobility; three studies investigated NMES-assisted cycling and demonstrated improved gross motor skills and walking distance or speed. Eleven studies investigated NMES-assisted gait and demonstrated improved muscle structure, strength, selective motor control, gross motor skills, and gait mechanics. Seven studies investigated NMES for spasticity reduction, and five of the seven studies demonstrated reduced spasticity.
1 Introduction

Cerebral palsy (CP) is the most common motor disability in childhood, affecting 1.5 to 4 per 1,000 live births and presenting as spastic, dyskinetic, and ataxic types of CP, depending on the location of early brain injury (Bax et al., 2005). Spastic CP is the most common type of CP characterized by four interrelated neuromuscular impairments associated with corticospinal tract injury: muscle weakness, short muscle-tendon length relative to bone, spasticity, and impaired selective motor control (SMC) (Bax et al., 2005; Wright M. et al., 2012; Zhou et al., 2017). Dyskinetic CP is characterized by involuntary muscle contractions imposed on purposeful movement, limiting functional mobility, and is thought to be associated with basal ganglia injury (Sanger, 2015). Ataxic CP impairs balance and coordination associated with an injury in the cerebellum of the brain (Imamura et al., 1992; Rankin et al., 2010). Depending on the location of brain injury, an individual may present with symptoms of more than one type of CP (Schiariti et al., 2018). This review focuses on neuromuscular electrical stimulation (NMES) application to augment lower limb exercise for individuals with spastic CP, affecting around 80% of children with CP (Novak, 2014; CDC, 2020). Spastic CP can involve unilateral or bilateral limbs. In milder cases of CP, the lower limb is more affected distally, than proximally. Functional mobility in spastic CP is described by the Gross Motor Function Classification System (GMFCS). GMFCS levels range from I to V, with GMFCS I being mild and GMFCS V being the most severe (Palisano et al., 2007), and are reported in this review.

NMES is an emerging assistive technology applied as surface stimulation through electrodes placed over the skin or directly to the muscle via implanted electrodes to initiate or augment skeletal muscle contraction through intact peripheral nerves (Mooney and Rose, 2019; Wright et al., 2012). NMES applied through surface electrodes is the most common application as it is a non-invasive technique and generally well tolerated (Mooney and Rose, 2019). Electrodes are commonly placed over the motor point where the motor nerve innervates the muscle (Botter et al., 2011). The application of NMES to achieve functional movements is often referred to as Functional Electrical Stimulation (FES) (Masani and Popovic, 2011). The application of low-intensity electrical stimulation primarily targeting nerves, referred to as Transcutaneous Electrical Nerve Stimulation (TENS), is routinely used for pain management and has the potential to improve motor function in patients with neurodegenerative disorders (Levin and Hui-Chan, 1992; Vance et al., 2012; Kroeling et al., 2013). NMES applications include the use of NMES-assisted strengthening, NMES-assisted gait, and NMES spasticity reduction.

NMES parameters that control stimulation vary based on clinical application, targeted muscles, and individual tolerance (Maffiuletti, 2010). Parameters reported in this review include stimulation frequency, intensity, pulse width, timing (on/off ratio), and ramp. The frequency of electrical stimulation refers to the number of times a pulse of current is applied within one second, measured in Hertz (Hz). Higher frequencies generally produce more muscle activation as long as the individual pulses reach muscle fibers after their refractory period, do not result in neurotransmitter depletion, or do not block nerves otherwise (e.g., nerve blocking with monophasic high-frequency stimulation or with charge-balanced kilohertz frequency alternating current), therefore, it generates more force and can lead to increased fatigue and lower tolerance (Chaudhuri and Behan, 2004; Gorgey et al., 2009; Wegrzyk et al., 2015). Intensity or pulse amplitude refers to the amount of current delivered, or the voltage applied to the electrodes (respectively resulting in change of the current delivered) during each pulse. It is measured in milliamperes (mA) for current-controlled and Volts for voltage-controlled stimulation, where the current is proportional to the voltage. Pulse width refers to the duration between the start and end of each electrical pulse and is typically reported in microseconds (μs). Longer pulse widths are associated with increased muscle force; however, shorter pulse widths may provide patients with more comfort and increased tolerance (Mogyoros et al., 1996; Knash et al., 2003; Mang et al., 2011, 2011). Timing (on/off) refers to the duration the stimulation with a given frequency is turned on versus turned off, typically reported in seconds, whereas ramp refers to the gradual increase followed by a gradual decrease in stimulation intensity to facilitate adaptation, reduce the

Conclusion: A growing body of evidence supports the use of NMES-assisted strengthening, NMES-assisted gait, and NMES for spasticity reduction to improve functional mobility for individuals with spastic CP. Evidence for NMES to augment exercise in individuals with spastic CP remains limited. NMES protocols and parameters require further clarity to translate knowledge to clinicians. Future research should be completed to provide richer evidence to transition to more robust clinical practice.

KEYWORDS

cerebral palsy, exercise, transcutaneous electric nerve stimulation, gait, neuromuscular electrical simulation
likeliness of discomfort, and promote smooth gradations of
tetany between different muscle groups (Baker et al., 2000; Bijak et al., 2005).

A growing body of evidence supports the use of NMES in the
treatment and care of individuals with CP (Mooney and Rose, 2019; Novak et al., 2020). In this review, treatments were
categorized into NMES-assisted strengthening exercises (therapeutic exercise and cycling), NMES-assisted gait (overground and treadmill walking for neuroprosthetic and
neurotherapeutic effects), and NMES for spasticity reduction
during strengthening exercise and gait which typically targets
spastic muscles with lower frequency stimulation using TENS
parameters). The ultimate goal of NMES for individuals with CP is to improve functional mobility and quality of life.

Muscle weakness is a common impairment in individuals with CP and significantly impacts their ability to function and participate in activities. Weakness is primarily caused by
neurological impairment, including reduced motor-unit firing
and by muscle structural changes including in the muscle
fascicles such as fatty replacement, in sarcomeres, and in
muscle fiber size variability (Huijing, 1998; Elder et al., 2003;
Lieber et al., 2004; Foran et al., 2005; Rose and McGill, 2005;
Maliaya et al., 2007; Stackhouse et al., 2007; Barber et al., 2012;
Noble et al., 2014; Zhou et al., 2017). Evidence indicates that use
of NMES for augmenting exercise increases microvascular perfusion
in the stimulated skeletal muscle (Clemente et al., 1991; Moloney et al., 2006; Bahadori et al., 2017). This decreases the diffusion
distance in the stimulated muscle tissue and enhances the
exchange of nutrients and metabolites between the blood and
tissue, improving physiological muscle function. Given the vital
role of muscle tissue (e.g., in maintaining stable glucose
metabolism), NMES might further benefit the overall quality of
life in individuals across all GMFCS levels.

Accurate interpretation of research requires relevant,
validated outcome measures. Therefore, this review includes
studies that report outcome measures recommended as
Common Data Elements (CDE) by The National Institute of
Neurological Disorders and Stroke (NINDS) (Grinnon et al., 2012). The CDE database is structured by diagnosis and includes
CDEs recommended for CP.

Using the NINDS CDE database, there are several ways to
measure and assess changes in strength in individuals with CP (Table 1). These include both direct strength measures, such as
Manual Muscle Testing and Maximum Voluntary Isometric
Contraction Testing, as well as measures of functional
mobility, such as temporal-spatial parameters of gait (Lee et al., 2008), 3D gait analysis of kinematics and kinetics
including the Gait Deviation Index (GDI) (Schwartz and
Rozumalski, 2008), 6 Minute Walk Test (6MWT) (Maher et al., 2008) which reflects gait distance, Timed Up and Go
(TUG) (Kaya Kara et al., 2019), and Gross Motor Function
Measure (GMFM) (Russell et al., 2000). Although not CDE
outcomes, dynamometry and timed sit to stand are often used
to reflect changes in muscle strength and function in
individuals with CP. Changes in muscle physiology can be
assessed indirectly through muscle structure using
musculoskeletal ultrasound (US) and Magnetic Resonance
Imaging (MRI). Our review also identified in certain
studies the CDE measures of Selective Control Assessment of
the Lower Extremity (SCALE) (Fowler et al., 2009) for
assessment of SMC.

This scoping review examines the application of NMES to
augment lower extremity exercises for individuals with spastic
CP, and reports the effects of NMES on neuromuscular
impairments and function in spastic CP, to provide a
foundation of knowledge that can guide research to advance
the field and provide more effective treatment.

2 Methods

Given the extent of the literature, we determined that the most
appropriate type of review for this field is a scoping review (Pollock et al., 2022). The primary goal of our review was to give
a comprehensive assessment of the current use of NMES for
augmenting exercise for individuals with spastic CP. We also
sought to identify knowledge gaps to guide future research
directions. The Preferred Reporting Items for Systematic Reviews
and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR)
checklist was utilized to guide this review (Tricco et al., 2018).

A literature search was completed using Scopus, Medline,
Embase, and CINAHL databases with additional publications
referenced through the primary search. The search was
completed on 2 November 2021, using the following
keywords and Boolean operators: “spastic cerebral palsy”
AND “neuromuscular electrical stimulation” OR
“functional electrical stimulation”. The inclusion criteria
for the articles were as follows: 1) the study involved
individuals with CP, 2) the study reported outcome
measures recommended by CDE for CP and were related
to muscle strength and function, gait temporal-spatial
parameters, and kinematics as identified in Table 1; 3) the
study incorporated a known NMES dosage (session, duration,
and frequency) with a known exercise component, such as
strengthening, cycling, gait training; 4) the study was
available in English; and 5) the study was published as a
full-text manuscript. The exclusion criteria for the articles
were as follows: 1) NMES was not a component of the study,
2) exercise was not a component of the study, 3) duration of
treatment period was less than 4 weeks or not reported; 4)
investigated muscles were not involving lower extremities; 5)
articles were from dissertations, conference posters, or
abstracts, 6) studies were published before 2001.

Using recommendations by the National Institute of
Neurological Disorders and Stroke (NINDS), the authors used
publications reporting at least one common data element (CDE)
outcome measures specific to the diagnosis of CP. Each publication was given a level of evidence based on the Oxford Centre for Evidence-Based Medicine 2011 Level of Evidence guidelines (Howick, 2011). Data were extracted by the authors (KG, CJ, KS, BB) for each publication but unblinded to the results of other authors.

3 Results

The initial 5-database search resulted in 168 publications, and an additional 41 articles were identified from references. Fifty-one articles were duplicates. The authors used titles and abstracts to screen the publications for the relevance of exercise programs involving the lower extremity. Fifty-seven articles were discarded due to diagnoses other than spastic CP or study aims outside the scope of exercise. One hundred and one articles, including seven review articles, met criteria and were fully reviewed by the authors; however, 68 were excluded upon further review for different populations (<sup>n</sup> = 5), absence of CDE for CP outcome measures (<sup>n</sup> = 6), lack of NMES intervention (<sup>n</sup> = 10), inadequate or unreported treatment duration (<sup>n</sup> = 10), lack of exercise component (<sup>n</sup> = 11), language other than English (<sup>n</sup> = 2), muscle groups other than lower extremities (<sup>n</sup> = 6), non-qualifying publication type (<sup>n</sup> = 15), and published before 2001 (<sup>n</sup> = 3). Based on these inclusion criteria, this scoping review includes a total of 33 articles, 26 intervention studies, and seven reviews. See Figure 1 for the publication search flow chart.

The literature was categorized by the application of NMES, including NMES-assisted strengthening, NMES-assisted gait, and NMES for spasticity reduction. Extracted variables included the study’s aim study design, age of participants, sample size, limb involvement (bilateral and/or unilateral), GMFCS level, device type, targeted muscle, NMES dose (number of weeks, sessions per week, and time per session), NMES parameters (frequency, intensity, pulse width, timing, ramp, waveform, and mode), and CDE outcomes recommended by NINDS, detailed in Tables 2–4.

3.1 Neuromuscular electrical stimulation-assisted strengthening

A total of fourteen articles were included for NMES-assisted strengthening, as shown in Table 2. NMES-assisted strengthening interventions included NMES augmenting therapeutic exercise, pre-operative surgical preparation, post-operative recovery, and NMES-assisted cycling. Several articles overlapped in the type of intervention, such as strengthening and spasticity reduction.

3.1.1 Neuromuscular electrical stimulation-assisted therapeutic exercise

Eleven studies reported NMES-assisted therapeutic exercise intervention: one case report (Daichman et al., 2003), one case series (Greve and Colvin, 2021), one pilot study (Stackhouse et al., 2007), two prospective trials (Nunes et al., 2008; Rajalaxmi...
et al., 2017), two prospective controlled studies (Karabay et al., 2015; Mukhopadhyay et al., 2017), and four randomized controlled trials (RCT) (Kerr et al., 2006; Khalili and Hajihassanie, 2008; Arya et al., 2012; Qi et al., 2018). Strengthening involved both home and clinic interventions using portable NMES devices with surface or implanted electrodes focused on the quadriceps, gastrocnemius, and tibialis anterior muscles. NMES was applied during positioning, stretching, facilitated exercises, strengthening, activities of daily living, balance, posture, and gait exercises (Daichman et al., 2003; Kerr et al., 2006; Stackhouse et al., 2007; Khalili and Hajihassanie, 2008; Nunes et al., 2008; Arya et al., 2012; Karabay et al., 2015; Mukhopadhyay et al., 2017; Rajalaxmi et al., 2017; Qi et al., 2018; Greve and Colvin, 2021). Dosage consisted of 15–60 min, one to seven times per week for 4–16 weeks. See Table 3 for specific NMES parameters and dosage for each study.

Ten studies using NMES-assisted therapeutic exercise reported improvements in muscle structure, strength, gross motor skills, WS, and functional mobility (Daichman et al., 2003; Stackhouse et al., 2007; Khalili and Hajihassanie, 2008; Nunes et al., 2008; Arya et al., 2012; Karabay et al., 2015; Mukhopadhyay et al., 2017; Rajalaxmi et al., 2017; Qi et al., 2018; Greve and Colvin, 2021). Two studies examined muscle cross-sectional area (CSA) using ultrasound or MRI and found an increase in CSA values of the quadriceps (Stackhouse et al., 2007), tibialis anterior (Karabay et al., 2015), and gastrocnemius (Karabay et al., 2015). Two studies reported an increase in quadriceps strength assessed with dynamometry (Daichman et al., 2003; Stackhouse et al., 2007). Six studies conducted the GMFM (Kerr et al., 2006; Nunes et al., 2008; Arya et al., 2012; Mukhopadhyay et al., 2017; Qi et al., 2018; Greve and Colvin, 2021), and four of the six studies reported positive changes in gross motor skills (Nunes et al., 2008; Mukhopadhyay et al., 2017; Qi et al., 2018; Greve and Colvin, 2021). Two studies reported improvement in functional mobility using the PEDI (Daichman et al., 2003) and FMS (Greve and Colvin, 2021). Studies also reported improvement in gait (Daichman et al., 2003; Arya et al., 2012; Mukhopadhyay et al., 2017; Rajalaxmi et al., 2017), WS (Stackhouse et al., 2007; Arya et al., 2012; Mukhopadhyay et al., 2017; Qi et al., 2018), and endurance (Greve and Colvin, 2021) following NMES. Five studies (Daichman et al., 2003; Kerr et al., 2006; Stackhouse et al., 2007; Khalili and Hajihassanie, 2008; Greve and Colvin, 2021) commented on adherence with 90–100% tolerance for using NMES by individuals participating in these studies. See Table 4 for CDE outcomes and results of each study.
| Intervention/ Authors (year) | NMES Intervention | Evidence Level | Study Design | Age (years) | Sample Size | GMFCS Level | Limbs | Muscle | NMES Duration (weeks) | Frequency of use (days/week) | Session duration (min) |
|-----------------------------|-------------------|----------------|--------------|-------------|-------------|-------------|-------|--------|-----------------------|--------------------------|---------------------|
| **Strengthening**           |                   |                |              |             |             |             |       |        |                       |                          |                     |
| Arya et al. (2012)          | Strengthening     | 2              | RCT          | 7-14        | 10          | -           | Bilateral, Unilateral | Quads, TA | 4                    | 4-5                       | 20-30                |
| Daichman et al. (2003)      | Strengthening, Spasticity Reduction | 4              | CR           | 13          | 1           | -           | Bilateral | Quads   | 6                    | 3-4                       | 5-15                 |
| Greve and Colvin, 2021      | Strengthening     | 4              | CS           | 9-15        | 3           | II          | Bilateral | Quads   | 6                    | 7                        | 15-30                |
| Karzbay et al. (2015)       | Strengthening, Spasticity Reduction | 3              | PCS          | 3-14        | 28          | I-V         | Bilateral | GS, TA  | 4                    | 5                        | 30                   |
| Kerr et al. (2006)          | Strengthening     | 2              | RCT          | 5-16        | 60          | -           | Bilateral | Quads   | 16                   | 5                        | 60                   |
| Khalili and Hajihassanie, 2008 | Strengthening, Spasticity Reduction | 2              | RCT          | 11-14       | 11          | -           | Bilateral | Quads   | 4                    | 3                        | 30                   |
| Mulpaddhyay et al. (2017)   | Strengthening     | 3              | PCS          | 7-14        | 26          | I-III       | Bilateral, Unilateral | TA      | 12                   | 5                        | 30                   |
| Nunes et al. (2008)         | Strengthening     | 3              | PT           | 7-15        | 10          | -           | Unilateral | TA      | 7                    | 1-2                      | 30                   |
| Qi et al. (2018)            | Strengthening     | 2              | RCT          | 4-9         | 100         | -           | -        | TA      | 6                    | 5                        | 20                   |
| Rajalaxmi et al. (2017)     | Strengthening, Spasticity Reduction | 3              | PT           | 5-10        | 30          | -           | Bilateral | TA      | 8                    | 5                        | 15-20                |
| Stackhouse et al. (2007)    | Strengthening     | 3              | PS           | 8-12        | 11          | II-III      | Bilateral | Quads, GS | 12                   | 3                        | 15/muscle            |
| Armstrong et al. (2020)     | Cycling           | 2              | RCT          | 6-18        | 21          | II-IV       | Bilateral, Unilateral | Gluteals, Quads, HS, GS, TA | 8                    | 3                        | 30                   |
| Johnston and Wainwright, 2011 | Cycling          | 4              | CR           | 49          | 1           | II          | Bilateral | Gluteals, Quads, HS, GS | 12                   | 3                        | 30                   |
| Özen et al. (2021)          | Cycling, Spasticity Reduction | 2              | RCT          | 4-12        | 25          | I-III       | Bilateral | Quads, HS, GS, TA | 4                    | 5                        | 30                   |
| **Gait**                    |                   |                |              |             |             |             |       |        |                       |                          |                     |
| Chan et al. (2004)          | Gait              | 4              | SSRD         | 4-11        | 12          | -           | Bilateral, Unilateral | GS      | 4                    | 3                        | 15                   |
| Damiano et al. (2013)       | Gait              | 3              | PT           | 8-19        | 14          | I-II        | Bilateral, Unilateral | TA      | 40                   | 7                        | 360                  |
| Gonçalves et al. (2019)     | Gait              | 4              | SSRD         | 4-7         | 4           | I-II        | Unilateral | GS      | 8                    | 3                        | 50                   |
| Johnston et al. (2004)      | Gait              | 3              | PT           | 6-12        | 17          | II-IV       | Bilateral | Hip Add, Gluteals, Quads, HS, GS, TA | 4                    | 5                        | 560                  |

(Continued on following page)
| Intervention/Authors (year) | NMES Intervention | Evidence Level | Study Design | Age (years) | Sample Size | GMFCS Level | Limbs | Muscle | NMES Duration (weeks) | Frequency of use (days/week) | Session duration (min) |
|---------------------------|-------------------|----------------|--------------|-------------|-------------|-------------|--------|--------|-----------------------|----------------------------|------------------------|
| Pool et al. (2014) (Pool et al., 2014) | Gait | 4 | SSRD | 5–18 | 12 | I-II | Unilateral | TA | 8 | 6 | ≥60 |
| Pool et al. (2015) | Gait, Spasticity Reduction | 2 | RCT | 5–18 | 32 | I-II | Unilateral | TA | 8 | 6 | ≥240 |
| Pool et al. (2016) | Gait | 2 | RCT | 5–18 | 32 | I-II | Unilateral | TA | 8 | 6 | ≥240 |
| Prosser et al. (2012) | Gait | 3 | PT | 7–19 | 19 | I-II | Unilateral | TA | 12 | 6 | 30–360 |
| Robinson et al. (2015) | Gait | 4 | CR | 57 | 1 | - | Bilateral | HS, TA | 6 | 5 | 480 |
| van der Linden et al. (2003) | Gait | 4 | CR | 57 | 1 | - | Bilateral | Gluteals | 6 | 5 | 480 |
| van der Linden et al. (2008) | Gait | 2 | RCT | 5–14 | 22 | - | Bilateral | Unilateral | Quads, TA | 10 | 6 | 60 |

### Spasticity Reduction

| Authors (year) | NMES Intervention | Evidence Level | Study Design | Age (years) | Sample Size | GMFCS Level | Limbs | Muscle | NMES Duration (weeks) | Frequency of use (days/week) | Session duration (min) |
|----------------|-------------------|----------------|--------------|-------------|-------------|-------------|--------|--------|-----------------------|----------------------------|------------------------|
| AlAbdulwahab and Al-Gabbani, 2010 | Spasticity Reduction | 3 | RCT | 7–12 | 42 | - | Bilateral | Hip Add | 1 | 7 | 3 × 15 |
| Daichman et al. (2003) | Strengthening, Spasticity Reduction | 4 | CR | 13 | 1 | - | Bilateral | Quads | 6 | 3–4 | 5–15 |
| Karabay et al. (2015) | Strengthening, Spasticity Reduction | 3 | PCS | 3–14 | 28 | I-V | Bilateral | GS, TA | 4 | 5 | 30 |
| Khalili and Hajhassanie, (2008) | Strengthening, Spasticity Reduction | 2 | RCT | 11–14 | 11 | - | Bilateral | Quads | 4 | 3 | 30 |
| Özen et al. (2021) (Özen et al., 2021) | Cycling, Spasticity Reduction | 2 | RCT | 4–12 | 25 | I-III | Bilateral | Quads, HS, GS, TA | 4 | 5 | 30 |
| Pool et al. (2015) | Gait, Spasticity Reduction | 2 | RCT | 5–18 | 32 | I-II | Unilateral | TA | 8 | 6 | ≥240 |
| Rajalaxmi et al. (2017) | Strengthening, Spasticity Reduction | 3 | PT | 5–10 | 30 | - | Bilateral | TA | 8 | 5 | 15–20 |

Level of Evidence (Howick, 2011). Study design abbreviations: Case Report (CR), Case Series (CS), Pilot Study (PS), Prospective Trial (PT), Prospective Controlled Study (PCS), Randomized Controlled Trial (RCT), Single Subject Research Design (SSRD). Muscle abbreviations: Gluteus Maximus and/ or Medius (Gluteals), Quadriceps (Quads), Tibialis Anterior (TA), Gastrocnemius & Soleus (GS), Hamstrings (HS). CDE, outcome measures abbreviations: Refer to Table 1. Other outcome measure abbreviations: Physiological Cost Index (PCI), Selective Motor Control (SMC), Australian Spasticity Assessment Scale (ASAS), Activities-specific Balance Confidence scale (ABC), Tinetti Performance Oriented Mobility Assessment (POMA).
3.1.2 Neuromuscular electrical stimulation-assisted cycling

Three studies reported NMES-assisted cycling for exercise, where multichannel NMES was applied using surface electrodes while the participant rode an indoor tricycle or stationary bicycle. One case report (Johnston and Wainwright, 2011) and two RCTs (Armstrong et al., 2020; Özen et al., 2021) reported on multichannel NMES used to target multiple muscles during cycling, including the gluteals, quadriceps, hamstrings, gastrocnemius, and/or anterior tibialis. NMES was applied during cycling alone or in addition to interventions, such as ROM, strengthening, and balance.

| Authors (year) | NMES frequency (Hz) | NMES intensity (mA) | NMES pulse width (μs) | NMES Timing [on/off] (sec) | NMES ramp [up/Down] (sec) | NMES Waveform | NMES mode |
|----------------|---------------------|---------------------|----------------------|-----------------------------|-----------------------------|---------------|-----------|
| AlAbdulwahab and Al-Gabbani, (2010) | 100 | Until tingling sensation | 250 | - | - | - | Constant |
| Armstrong et al. (2020) | 40–50 | Tolerance | 200–250 | - | - | - | - |
| Arya et al. (2012) | 20–40 | Tolerance | 200 | 14/5 | 3 | Biphasic | Alternate |
| Chan et al. (2004) | 30–35 | Visible muscle contraction | - | - | - | - | Manually triggered during stance |
| Dachman et al. (2003) | 35 | Tonic contraction | 300 | 10/50 | 2 | - | - |
| Damiano et al. (2013) | 25 | - | 25–50 | - | - | Asymmetric, Biphasic | Timed with gait |
| Gonçalves et al. (2019) | 26–30 | 17–33 | 300 | - | - | Symmetric | Manually triggered during activities |
| Greve and Colvin, (2021) | 35 | 9.75–32.5 | 200–350 | 5–10/10–30 | 1–2 | Symmetric, Biphasic | Synchronous |
| Johnston et al. (2004) | 20 | 20 | 200 | 2–4/0 | 1–3 | Asymmetric, Biphasic | - |
| Johnston and Wainwright, (2011) | 33 | 40–80 | 250 | - | - | - | - |
| Karabay et al. (2015) | 25 | 20–30 | 250 | 10/12 | - | - | - |
| Kerr et al. (2006) (Kerr et al., 2006) | 35 | Tolerance | 300 | 7/12 | 2/1 | - | - |
| Khalili and Hajhassanie, (2008) | 30 | Visible muscle contraction | 400 | 4/4 | 0.5 | - | - |
| Mukhopadhyay et al. (2017) | 40 | 0–30 | 200 | - | - | Biphasic | - |
| Nunes et al. (2008) | 50 | 28–44 | 250 | 5/10 | - | - | - |
| Özen et al. (2021) | 30–45 | 100 | 250–300 | - | 7/2 | Biphasic | - |
| Pool et al. (2014) | 33 | Tolerance | 300 | - | - | Asymmetric, Biphasic | - |
| Pool et al. (2015) | 33 | - | 25–100 | - | - | Asymmetric, Biphasic | - |
| Pool et al. (2016) | 33 | - | 25–100 | - | - | Asymmetric, Biphasic | - |
| Prosser et al. (2012) | 16.7–33 | - | 25–300 | - | - | Asymmetric, Biphasic | Timed with gait |
| Qi et al. (2018) | - | Visible muscle contraction | - | - | - | - | Constant |
| Rajalaxmi et al. (2017) | - | - | - | - | - | Symmetric, Biphasic | Timed with gait |
| Robinson et al. (2015) | 30–40 | Tolerance | 200–300 | - | - | Symmetric, Biphasic | - |
| Stackhouse et al. (2007) | 50 | 20 | 5–200 | 15/45 | 3 | - | Alternate |
| van der Linden et al. (2003) | 10–30 | - | 75–100 | 5/10–15 | 0.8 | Asymmetric, Biphasic | - |
| van der Linden et al. (2008) | 10–40 | 20–70 | 3–350 | 6/10–14 | 0.8 | Asymmetric, Biphasic | Triggered during gait |
| Authors (year) | CDE Outcome measures | Change in CDE outcome measures relative to control | Other Outcome measures | Change in other outcome measures relative to control |
|----------------|----------------------|------------------------------------------------|------------------------|--------------------------------------------------|
| AlAbdulwahab and Al-Gabbani, (2010) | WS | WS ↑ (p < 0.021), Step length ↑ (p < 0.008) | Visual observations of knee positions (improved) | Visual observations of knee positions (improved) ↑ |
| Armstrong et al. (2020) | GMFM | GMFM ↑ (p < 0.001) | Sit to Stand | |
| Arya et al. (2012) | WS | WS: 7.83 m/min (p < 0.01) ↑ | Physiological Cost Index (PCI) | PCI: 1.83 (p < 0.001) ↓ |
| Chan et al. (2004) | IGA | IGA ↑ (Improved ankle power p < 0.015) | | |
| Daichman et al. (2003) | SAGV | SAGV (walking velocity, step length, and cadence) ↑ | Range of motion (ROM) | ROM ↑ (popliteal angle decreased from 40 to 35°) |
| Damiano et al. (2013) | US | TA (US) CSA ↑ | | |
| Gonçalves et al. (2019) | WS | WS ↑, GMFM ↑ | | |
| Greve and Colvin, (2021) | 6MWT | 6MWT ↑ (above MCID) | | |
| Johnston et al. (2004) | SAGV | SAGV (Walking velocity, step length, and cadence) ↑ (p < 0.05) | ROM | ROM ↑ (p < 0.05) |
| Johnston and Wainwright, (2011) | 6MWT | 6MWT (didn’t meet MDC) | | |
| Kerr et al. (2006) | GMFM | GMFM (no change) | Dynamometer | Dynamometer (no change) |
| Khalili and Hajhassanie, (2008) | MAS | MAS ↓ (2.0 compared to 1.2 in the control group; p = 0.046) | ROM | ROM ↑ (from 9 to 15°, p = 0.04) |
| Mukhopadhyay et al. (2017) | WS | WS ↑ (17.67%) | PCI | PCI ↓ (19.7%) |
| Nunes et al. (2008) | GMFM | GMFM ↑ (group 1: from 94.28% to 97.14% p < 0.05, group 2: from 95.23% to 98.09% p < 0.05) | TA muscle strength of ↑ (manual) | |

(Continued on following page)
| Authors (year) | CDE Outcome measures | Change in CDE outcome measures relative to control | Other Outcome measures | Change in other outcome measures relative to control |
|---------------|----------------------|--------------------------------------------------|-----------------------|--------------------------------------------------|
| Özen et al. (2021) | 6MWT | 6MWT ↑ | GMFM ↑ | Visual Gait Analysis | Visual Gait Analysis ↑ (improvement in ankle dorsiflexion and foot contact) |
|                  | GMFM ↑ |                      |                      |                                                  |
|                  | WooFIM ↑ |                      |                      |                                                  |
|                  | MAS ↓ |                      |                      |                                                  |
|                  | Tardieu Scale ↓ |                      |                      |                                                  |
| Pool et al. (2014) | OGS | OGS (no change) |                      |                                                  |
|                  | ROM |                      |                      |                                                  |
|                  | Dynamometry |                      |                      |                                                  |
|                  | ASAS ↑ (p < 0.01) |                      |                      |                                                  |
|                  | SMC dorsiflexion grade ↑ | (Boyd and Graham, 1999) |                      |                                                  |
|                  | WeeFIM ↑ |                      |                      |                                                  |
|                  | MAS ↑ |                      |                      |                                                  |
|                  | Tardieu Scale ↑ |                      |                      |                                                  |
| Pool et al. (2015) | IGA | IGA ↑ |                      |                                                  |
|                  | Tardieu Scale ↑ |                      |                      |                                                  |
|                  | - ankle angle ↑ (mean difference 11.9°, 95% CI 6.8°–17.1°, p < 0.001) |                      |                      |                                                  |
|                  | - stance ↑ (mean difference 0.27, 95% CI 0.05–0.49, p = 0.011) |                      |                      |                                                  |
|                  | - step length ↑ (mean difference 0.06, 95% CI 0.03–0.126, p = 0.035) |                      |                      |                                                  |
|                  | Tardieu Scale ↑ (dynamic ankle dorsiflexion range mean difference 6.9°, 95% CI 0.4°–13.6°, p = 0.035) |                      |                      |                                                  |
| Pool et al. (2016) | MRI | MRI ↑ (TA muscle volume, p = 0.039) |                      |                                                  |
|                  | SCALE ↑ (mean difference 0.81, 95% CI 0.3–1.32, p < 0.001) |                      |                      |                                                  |
|                  | Dynamometry |                      |                      |                                                  |
|                  | - TA strength ↑ (p = 0.002) |                      |                      |                                                  |
|                  | - Ankle SMC ↑ (median difference 0.5, IQR 0–1, p = 0.048) |                      |                      |                                                  |
| Prosser et al. (2012) | IGA | IGA ↑ |                      |                                                  |
|                  | - (mean and peak dorsiflexion during swing and at foot-floor contact) | WS (no change) |                      |                                                  |
| Qi et al. (2018) | WS | WS ↑ (0.72 m/s vs. 0.57 m/s, p < 0.05) |                      |                                                  |
|                  | GMFM ↑ |                      |                      |                                                  |
| Rajalaxmi et al. (2017) | MAS | MAS ↑ (p < 0.001) |                      |                                                  |
|                  | Cadence ↑ |                      |                      |                                                  |
| Robinson et al. (2015) | OGS | OGS ↑ (from 12/22 to 19/22 [right], 14/22 to 21/22 [left]) |                      |                                                  |
|                  | Activity-specific Balance Confidence (ABC) Scale ↑ | (from 32.8% to 48.1%), |                      |                                                  |
|                  | Performance Oriented Mobility Assessment (POMA) ↑ | (from 12/28 to 15/28), |                      |                                                  |
| Stackhouse et al. (2007) | MRI | MRI ↑ (CSA of Quads +4.42 cm², p = 0.023) |                      |                                                  |
|                  | WS | WS ↑ (p = 0.028) |                      |                                                  |
| van der Linden et al. (2003) | IGA | IGA (no change) |                      |                                                  |
|                  | GMFM ↑ (not significant) |                      |                      |                                                  |
| van der Linden et al. (2008) | IGA | IGA ↑ (p < 0.01) |                      |                                                  |
|                  | WS ↑ (0.03 m/s, p < 0.05) |                      |                      |                                                  |

Common data elements (CDE) by the national institute of neurological disorders and stroke (NINDS).
NMES intervention dosage ranged from 30 min, 3–5 times per week for 4–12 weeks.

Three studies using NMES-assisted cycling reported boosting gross motor skills, walking distance, and speed (Johnston and Wainwright, 2011; Armstrong et al., 2020; Özen et al., 2021). Two studies (Armstrong et al., 2020; Özen et al., 2021) reported improvement in gross motor skills assessed with the GMFM. Studies also reported an increase in walking distance assessed with 6MWT (Johnston and Wainwright, 2011; Özen et al., 2021) and speed assessed using the TUG (Johnston and Wainwright, 2011). NMES was well-tolerated in one study (Özen et al., 2021) and variable in two studies (Johnston and Wainwright, 2011; Armstrong et al., 2020). See Tables 2, 3, 4 for details of each study’s NMES application and CDE outcomes.

### 3.2 Neuromuscular electrical stimulation-assisted gait

Table 2 reports the results of NMES-assisted gait, which includes interventions using NMES during gait for treadmill or overground walking with a known therapeutic dosage.

Eleven studies reported NMES-assisted gait for strengthening and improving gait pattern, including one case report (Robinson et al., 2015), three single-subject research design studies (SSRD) (Chan et al., 2004; Pool et al., 2014; Gonçalves et al., 2019), three prospective trials (Johnston et al., 2004; Prosser et al., 2012; Damiano et al., 2013), and four RCTs (Pool et al., 2016; 2015, 2014; van der Linden et al., 2003, 2008). Various NMES devices were used, including surface electrodes for non-wearable units targeting the gluteals, quadriceps, gastrocnemius, and tibialis anterior. Wearable units targeted hip adductors, quadriceps, hamstrings, gastrocnemius, and tibialis anterior. NMES was applied during walking overground or performing functional task training. Only one study applied NMES while on a treadmill (Chan et al., 2004). NMES dosage ranged from 15 min to 8 h per day, 3–7 days per week for 4–40 weeks. See Table 3 for details of each study’s NMES application and parameters.

The eleven studies that investigated NMES-assisted gait found improved muscle structure, strength, SMC, gross motor skills, and gait (van der Linden et al., 2003, 2008; Chan et al., 2004; Johnston et al., 2004; Prosser et al., 2012; Damiano et al., 2013; Pool et al., 2016, 2015, 2014; Robinson et al., 2015; Gonçalves et al., 2019). NMES-assisted gait resulted in increased muscle volume of tibialis anterior as assessed on MRIs (Pool et al., 2016), increased tibialis anterior CSA as assessed on ultrasound (Damiano et al., 2013), increased strength as assessed by dynamometers (Pool et al., 2016, 2014), improved SMC as assessed by SCALE (Pool et al., 2016), improved gross motor skills as assessed by GMFM (van der Linden et al., 2003; Chan et al., 2004; Johnston et al., 2004; Gonçalves et al., 2019), and improved gait as assessed by kinematics, kinetics, and temporal-spatial parameters (Chan et al., 2004; Johnston et al., 2004; van der Linden et al., 2008; Prosser et al., 2012; Pool et al., 2015; Robinson et al., 2015). Compliance was reported to be high for NMES intervention (Chan et al., 2004; Prosser et al., 2012; Pool et al., 2016, 2015). Tolerance was reported as ranging from good (Damiano et al., 2013; Pool et al., 2014) to variable (van der Linden et al., 2003, 2008). See Table 4 for CDE outcome measures and results for each NMES-assisted gait study.

### 3.3 Neuromuscular electrical stimulation for spasticity reduction

Seven studies reported on the effects of NMES on spasticity. One case report (Daichman et al., 2003), one prospective controlled study (Karabay et al., 2015), one prospective trial (Rajalaxmi et al., 2017), and four RCTs (Khalili and Hajihassanie, 2008; AAlAbdulwahab and Al-Gabbani, 2010; Pool et al., 2015; Özen et al., 2021). The targeted muscles for NMES included hip adductors, quadriceps, hamstrings, gastrocnemius, and tibialis anterior. NMES was applied to the antagonist muscle during exercises, including ROM, balance, strengthening, and gait training (Daichman et al., 2003; Khalili and Hajihassanie, 2008; Pool et al., 2015; Rajalaxmi et al., 2017; Özen et al., 2021). TENS was applied to the antagonist muscle during ROM and gait training exercises (AAlAbdulwahab and Al-Gabbani, 2010). In addition, NMES-assisted strengthening and NMES-assisted gait were investigated (Pool et al., 2015; Özen et al., 2021). The dosage varied between 5 and 240 min per session, 3–7 days per week for 1–8 weeks.

Among the seven studies of NMES for spasticity reduction, five studies reported reduced spasticity in the antagonistic muscle when using electrical stimulation (Khalili and Hajihassanie, 2008; AAlAbdulwahab and Al-Gabbani, 2010; Pool et al., 2015; Rajalaxmi et al., 2017; Özen et al., 2021). Study results included decreased resistance of the hip adductors (AAlAbdulwahab and Al-Gabbani, 2010), hamstrings (Khalili and Hajihassanie, 2008; Özen et al., 2021), and gastrocnemius muscles (Pool et al., 2015; Rajalaxmi et al., 2017; Özen et al., 2021) assessed by the Modified Ashworth Scale (MAS) or Tardieu Scale; while two studies found no change in spasticity (Daichman et al., 2003; Karabay et al., 2015). Application and results of NMES-assisted spasticity reduction can be found in Tables 2, 3, 4.

### 3.4 Additional literature

Our search identified seven studies reviewing NMES as an intervention for individuals with CP, including reviews (Khamis et al., 2018; Wright M. et al., 2012), scoping reviews (Mooney and Rose, 2019; Walhain et al., 2021), and systematic reviews with meta-analysis (Salazar et al., 2019) and without meta-analysis (Chiu and Ada, 2014; Moll et al., 2017). These reviews explicitly...
focused on the effects of NMES on muscle morphology (Walhain et al., 2021), gait (Mooney and Rose, 2019, p. 2; Wright P. A. et al., 2012), gross motor function (Salazar et al., 2019), ankle dorsiflexion (Moll et al., 2017), activities (Chiu and Ada, 2014), and improvement in gait deviations when using FES (Khamis et al., 2018). None of the listed reviews were specific to our scoping review looking at the NMES application as a lower extremity exercise for individuals with spastic CP.

4 Discussion

The findings of this scoping review indicate that NMES applied to strengthening exercise, gait, and spasticity reduction demonstrate potential benefits for improving muscle physiology, neuromuscular impairments, gait patterns, and functional mobility in individuals with spastic CP. The twenty-six intervention publications, dating from 2003 to 2021, included a total of 558 individuals aged 3–57 years with CP, GMFCS levels I-IV with unilateral or bilateral involvement. The dosage of NMES intervention varied by study, as noted in Table 2. In addition, while using NMES, the exercise activities varied and included ROM, strengthening (i.e., isometric contractions, progressive resistance exercises, cycling), positioning, functional tasks, and gait. NMES included both wearable and non-wearable devices with surface electrodes, with the exception of two studies that utilized implanted electrodes (Johnston et al., 2004; Stackhouse et al., 2007).

The NMES parameters utilized in these studies included frequencies between 10 and 50 Hz, stimulation intensities between 4 and 100 mA, with typical values below 40 mA, and pulse width between 3 and 350 μs, as shown in Table 3. The most substantial variation was in pulse width, which could be attributed to individual preferences and tolerances and to the sequence of adjusting NMES parameters during treatment. Although pulse width affects muscle force production, currently, there is no evidence suggesting the range of optimal pulse width, therefore, more studies are needed. Clinical experience suggests that electrode size and adherence to the skin and pulse width contribute most to NMES comfort level.

4.1 Neuromuscular electrical stimulation-assisted strengthening

NMES-assisted strengthening was found to increase strength, WS, walking distance, gross motor skills, and functional mobility. Three studies reported that NMES applied during exercise provided better outcomes than exercise alone (Khalili and Hajihassanie, 2008; Arya et al., 2012; Qi et al., 2018). This may be attributed to increased sensory attention to task and motor learning. Weaker muscles are likely to gain more from NMES strengthening than stronger muscles. Physical therapy, as well as surgical preparation and recovery, provide opportunities to initiate NMES strengthening of weakened muscles. Clinical expertise suggests that voluntary contraction is an important element of strengthening and motor control versus NMES stimulation alone. The results of this scoping review found further evidence that supports the use of NMES-assisted strengthening as a clinical treatment for individuals with spastic CP. Future studies need to study the impact of NMES-assisted strengthening on biological aspects of muscle physiology and chronic health conditions in individuals with spastic CP.

Another benefit to muscle strengthening is increasing overall muscle-tendon length across the joint, which may improve ROM (Zhou et al., 2017). Increasing muscle fiber diameter through strengthening theoretically increases overall muscle-tendon length due to the diagonal muscle fiber pennation angle relative to the axis of the bone (Zhou et al., 2017). Several studies identified that muscle CSA was increased with NMES-assisted strengthening, which likely would translate to increased overall muscle-tendon length and improved ROM (Stackhouse et al., 2007; Karabay et al., 2015). Future studies need to examine the impact of NMES-assisted strengthening on overall muscle-tendon length and joint ROM.

4.2 Neuromuscular electrical stimulation-assisted gait

NMES-assisted gait was found to improve strength, motor control, gait pattern, and temporal-spatial parameters. Similar to NMES-assisted strengthening, the repetitive movement of walking on a treadmill combined with NMES was found to have an advantage over treadmill gait or NMES alone for improving ankle power and gross motor skills of standing and walking (Chan et al., 2004). Furthermore, another study suggested that intensive use of NMES-assisted gait in home and community settings may facilitate motor learning (Pool et al., 2014). The results of this scoping review further strengthen the evidence to support NMES-assisted gait as a clinical treatment for individuals with spastic CP. Wearable single-channel NMES units are widely available and allow for home and community use to improve foot clearance in swing; however wearable multi-channel units are not widely available. Wearable multi-channel units are needed to treat gait abnormalities other than limited foot clearance in swing. Further research and development are needed in this area.

4.3 Neuromuscular electrical stimulation for spasticity reduction

NMES was also found to reduce spasticity, as assessed by Tardieu or MAS in five of seven studies reviewed; one study used
TENS (Al-Abdulwahab and Al-Gabbani, 2010), and four studies used NMES (Khalili and Hajihassanie, 2008; Pool et al., 2015; Rajalaxmi et al., 2017; Özen et al., 2021). Corticospinal tract injury results in a loss of descending neural signal activation and inhibition. Muscle spasticity is a neuromuscular impairment that results from loss of inhibition. Further research needs to investigate the potential inhibitory effects of NMES and how to optimize spasticity reduction and duration of treatment effects. The location of ideal electrode placement along the lumbar spine, over relevant dermatomes, directly over spastic muscle, or to elicit antagonist inhibition requires further research.

4.4 Limitations and future research

Limitations of this scoping review include the exclusion of some NMES-related studies that did not meet inclusion criteria due to NMES treatment duration of fewer than 4 weeks, the absence of an exercise component, technology development trials for NMES-assisted gait on a treadmill (Zahradka et al., 2021) or robotics (Shideler et al., 2020). These limitations may have eliminated some evidence in the field. However, with respect to treatment duration, a recent publication recommended at least 8–20 weeks of exercise training to facilitate meaningful changes in muscle structure and improve function in individuals with CP (Moreau and Lieber, 2022). This suggests that 8–20 weeks of exercise duration may be required, and therefore, it is possible that some of the studies in our review lacked the proper dosage to produce a meaningful change. While 11 out of 26 studies in this scoping review were RCTs, further studies with larger sample sizes and more consistent protocols using CDE outcome measures are needed to move the field forward.

This scoping review indicates that further research is needed to determine optimal NMES protocols and dosage using sensitive CDE outcome measures. Furthermore, device development of wearable NMES units that can be easily applied for NMES-assisted strengthening, gait, and spasticity reduction is needed for individuals with spastic CP. Understanding the relationship between NMES strength training and functional results, as well as the optimal NMES protocol and dosage, requires research with a larger sample size and longer treatment duration (i.e., 8–20 weeks). Identifying changes in neuromuscular impairments of weakness, short-muscle tendon unit, spasticity, and impaired SMC as well as motor learning, and utilizing CDEs with careful attention to minimal clinically important differences will allow us to better comprehend the therapeutic effects of NMES. Finally, advancing new NMES technology, such as wireless multichannel NMES devices and hybrid robotic and exoskeleton NMES systems, will provide evidence-based, clinically feasible interventions for individuals with CP to improve functional mobility.

5 Conclusion

Findings from this scoping review provide evidence that supports the use of NMES-assisted strengthening with therapeutic exercise and cycling, NMES-assisted gait, and NMES for spasticity reduction to improve mobility in individuals with spastic CP, based on validated CDE outcome measures. Wearable and non-wearable units were utilized with surface or implanted electrodes targeting the gluteals, hip adductors, hamstrings, quadriceps, gastrocnemius, and tibialis anterior to augment exercise and mobility. NMES was found to improve muscle structure, strength, gross motor skills, gait kinematics, WS, and walking distance and reduce spasticity. Clinicians can consider NMES to be an effective treatment for individuals with spastic CP. Additional research is needed to further investigate optimal parameters, dosage, and impact of NMES on neuromuscular impairments and functional mobility in individuals with spastic CP.

Author contributions

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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