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Wide-pulse-high-frequency neuromuscular electrical stimulation in cerebral palsy

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HIGHLIGHTS

- Similar Hmax/Mmax ratio was observed between cerebral palsy patients and healthy individuals.
- Extra-force production could be observed in response to both constant and burst-like frequency stimulations in both cerebral palsy and healthy individuals.
- High individual variability was observed in both cerebral palsy and healthy individuals in response to wide-pulse-high-frequency stimulation.

ABSTRACT

Objective: The present study assesses whether wide-pulse-high-frequency (WPHF) neuromuscular electrical stimulation (NMES) could result in extra-force production in cerebral palsy (CP) patients as previously observed in healthy individuals.
Methods: Ten CP and 10 age- and sex-matched control participants underwent plantar flexors NMES. Two to three 10-s WPHF (frequency: 100 Hz, pulse duration: 1 ms) and conventional (CONV, frequency 25 Hz, pulse duration: 50 μs) trains as well as two to three burst-like stimulation trains (2 s at 25 Hz, 2 s at 100 Hz, 2 s at 25 Hz; pulse duration: 1 ms) were evoked. Resting *soleus* and *gastrocnemii* maximal H-reflex amplitude (Hmax) was normalized by maximal M-wave amplitude (Mmax) to quantify α-motoneuron modulation.
Results: Similar Hmax/Mmax ratio was found in CP and control participants. Extra-force generation was observed both in CP (+18 ± 74%) and control individuals (+94 ± 124%) during WPHF ($p < 0.05$). Similar extra-forces were found during burst-like stimulations in both groups (+108 ± 110% in CP and +65 ± 85% in controls, $p > 0.05$).
Conclusion: Although the mechanisms underlying extra-force production may differ between WPHF and burst-like NMES, similar increases were observed in patients with CP and healthy controls.
Significance: Development of extra-forces in response to WPHF NMES evoked at low stimulation intensity might open new possibilities in neuromuscular rehabilitation.

Abbreviations: CONV, conventional stimulation modality (25 Hz–50 μs); CP, cerebral palsy; GL, *gastrocnemius lateralis*; GM, *gastrocnemius medialis*; GMFCS, Gross Motor Function Classification System; Hmax, maximal H-reflex amplitude; Hmax/Mmax, ratio between maximal H-reflex amplitude and maximal M-wave amplitude; Mmax, maximal M-wave amplitude; MVC, maximal voluntary contraction; NMES, neuromuscular electrical stimulation; SD, standard deviation; SE, standard error; Sol, *soleus*; WPHF, wide-pulse-high-frequency stimulation modality (100 Hz–1 ms).

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1. Introduction

Cerebral palsy (CP) is caused by abnormal or disrupted brain development affecting motor control centers. It leads to muscle pathologies (Barrett and Lichtwark, 2010) resulting in muscle weakness defined as a reduced maximal voluntary force (Elder et al., 2003; Engsberg et al., 2000; Wiley and Damiano, 1998). Adults with CP ascribe their functional deterioration to muscle force loss (Peterson et al., 2013). In accordance with CP patients' perception, reduced maximal voluntary contraction (MVC) force was objectively documented for lower limb muscle groups (Brouwer et al., 1998; Elder et al., 2003; Engsberg et al., 2000; Hussain et al., 2014; Leunkeu et al., 2010; Moreau et al., 2008; Rose and McGill, 2005; Stackhouse et al., 2005; Tammik et al., 2007; Wiley and Damiano, 1998) and associated with an impaired quality of life (Malone and Vogtle, 2010; Opheim et al., 2009), such as progressively reduced walking abilities (Jahnsen et al., 2004; Opheim et al., 2009). In CP patients classified as level II (children presenting walking limitations outdoor but able to walk without assistive devices) and III (children walking with an assistive device) on the "Gross Motor Function Classification System (GMFCS)" (Andersson and Mattsson, 2001; Palisano et al., 1997), MVC forces of lower limb muscle groups were almost equal to the forces required for walking (Dallmeijer et al., 2011). Consequently, even a slight loss of strength could lead to decreased walking capacity (Dallmeijer et al., 2011). Taken together, the reduced mobility in patients with CP aggravates muscle weakness, and, at the same time, increases the risk of cardiometabolic disease due to inactivity (Strauss et al., 1999).

Due to the insufficient "muscle force reserve" (Dallmeijer et al., 2011), it is important to preserve and possibly increase strength in this patient population. Neuromuscular electrical stimulation (NMES) could constitute a good adjunct training and rehabilitation paradigm in order to improve muscle force (Maffiuletti, 2010). Conventional (CONV) NMES patterns typically use a frequency between 20 and 50 Hz and a pulse duration between 50 and 400 μs (Collins, 2007). Such NMES patterns lead to random recruitment order and synchronous depolarization of motoneuron terminal branches inducing rapid development of fatigue (Maffiuletti, 2010). Such non-physiological motor unit recruitment might thus limit the potential benefit of NMES strengthening programs (Maffiuletti et al., 2011). Nevertheless, several of the few studies that assessed the effect of NMES training on muscle strength in patients with CP reported increased muscle force (Hazlewood et al., 1994; Kamper et al., 2006; Ozer et al., 2006; Stackhouse et al., 2007; van der Linden et al., 2003). Recently, a new NMES modality, using wider pulses (1 ms duration), has gained popularity in healthy (Bergquist et al., 2011a; Collins et al., 2001; Lagerquist et al., 2012) as well as in clinical populations (Clair-Auger et al., 2012, 2013). With this new wide-pulse-high-frequency (WPHF) NMES modality, a so-called "extra-force" has been observed with low stimulation intensities (Collins et al., 2001; Bergquist et al., 2011a, 2012; Dean et al., 2007; Lagerquist et al., 2009, 2012; Frigon et al., 2011). This extra-force has been proposed to be the result of a centrally-mediated motor unit recruitment through the activation of large diameter afferents in addition to the direct depolarization of the motoneurons axonal terminal branches (Bergquist et al., 2011b). However, this central origin has been challenged by Frigon et al. (2011) who reported a possible role for intramuscular factors in extra-force production. Whatever the underlying mechanisms, extra-force production is characterized by a gradual force increase over time during constant-frequency stimulation patterns and by the presence of a sustained force during burst-like frequency patterns (i.e. incorporation of a high frequency train within a low frequency pattern resulting in greater force evoked by a low frequency train following a high frequency bout). Noteworthy, in post-stroke patients, signs of extra-force were observed following burst-like WPHF but not during constant WPHF (Clair-Auger et al., 2012).

A hallmark of CP is spasticity, which is defined as a velocity-dependent increase in the stretch reflex (Brouwer et al., 1998; Poon and Hui-Chan, 2009). This reflex enhancement is reported to be due to an imbalance between inhibition and excitation at Ia – α-motoneuron synapses (i.e. reduced pre-synaptic inhibition) (Dietz, 2008). The balance between excitation and inhibition mechanisms at Ia – α-motoneuron synapses can be evaluated through the electrically induced Hoffmann reflex (H reflex) (Schieppati, 1987). Therefore if WPHF stimulations rely on large diameter afferents, it could be hypothesized that, by taking advantage of this increased reflex excitability, WPHF would evoke greater force in patients with CP in comparison to CONV. Additionally, if involvement of the spinal cord via large diameter afferents exist, some motoneurons would be activated according to the size principle (Henneman et al., 1965). Thus for a given force development, proportionally more slow, fatigue resistant type I fibers will be recruited than fast fatigable type II fibers. This additional orderly motor unit recruitment might lead to more fatigue-resistant evoked contractions (Bergquist et al., 2014). Therefore, the objective of this study was to assess the mechanical responses to WPHF-induced isometric plantar flexor contractions in CP patients. As Clair-Auger et al. (2012) observed a different behavior in response to burst-like and constant WPHF stimulation patterns, both were tested. We expected that: (1) patients with CP would present signs of extra-force when stimulated with both constant and burst-like WPHF modalities, and that (2) extra-force would be greater in patients with CP than in their healthy peers and would correlate with increased H-reflex amplitudes.

2. Material and methods

2.1. Subjects

Ten individuals suffering from CP and not taking any spasticity medication (5 women–5 men, 20.4 ± 4.7 years old, age range: 15 years and 9 months–30 years and 7 months) and 10 age- and sex-matched control individuals (5 women–5 men, 20.3 ± 4.5 years old, 15 years and 2 months–29 years and 3 months) volunteered to participate in this study after having been informed of the experimental procedures. CP patients were recruited from the database of the Willy Taillard laboratory of kinesiology of the University Hospitals of Geneva. Inclusion criteria for the patients with CP were as follows: (1) age 15–30 years old, (2) GMFCS between levels I and III, (3) no botulinum toxin injections in the previous 6 months, (4) no lower limb surgery in the previous year. Five patients were diplegic and 6 were hemiplegic (5 right side and 1 left side). Control individuals were recruited from the experimenters' entourage and were healthy and physically active. The study protocol was approved by the Ethics Committee of the University Hospitals of Geneva (protocol 12-026) and was performed in agreement with the declaration of Helsinki. All participants gave a written consent before participation. For under-eighteen participants, a parent (legal representative) also signed a written consent form.

2.2. Experimental protocol

Upon the participants' arrival, anthropometric measurements were performed. The most affected leg for diplegic CP patients, or the affected leg for hemiplegic CP patients was investigated, whereas the dominant leg was tested in control individuals (i.e.