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ORIGINAL ARTICLE

An acoustic myography functional assessment of cerebral palsy subjects compared to healthy controls during physical exercise

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Abstract

Individuals with cerebral palsy (CP) participate in reduced levels of physical activity and spend an increased amount of time in a sedentary state compared with healthy control subjects. Whether this in part can be explained by impaired muscle function is still unclear. The aim of the present study was to elucidate differences in muscle fibre recruitment during treadmill exercise between CP subjects and healthy age-, sex- and BMI-matched controls. This is a case–control study. Acoustic myography (AMG), a method recording fibre use and efficiency from contracting muscles, was applied during a period of treadmill exercise. The recorded AMG parameters revealed that the CP subjects had a significantly lower initial S-score (spatial summation) than the controls ($P < 0.01$). However, the T-score (temporal summation) and the E-score (efficiency) showed no significant differences between individuals with CP and the healthy control subjects. The present findings indicate that CP subjects use a higher degree of spatial summation (more fibres recruited) to keep up the same speed during treadmill exercise when compared to healthy matched control subjects. Our results suggest that individuals with CP have a tendency to recruit far more muscle fibres during bouts of exercise than healthy individuals. This may partly explain why CP subjects experience premature fatigue.

Keywords Cerebral palsy · Muscle fatigue · Muscle fibre activity · Acoustic myography

Clinical relevance: The present results represent an exciting new aspect for clinicians regarding what determines muscle activation during exercise in people with neurological disorders.
What is known about the subject: It is known that patients with neurological disorders fatigue very quickly during exercise, but the mechanisms behind this increased fatigue ability are unclear.
What the study adds to existing knowledge: The present study shows, that a higher number of fibres are recruited in CP muscles for any given muscle contraction. This may partly explain why CP subjects experience premature fatigue.

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Introduction

Cerebral palsy (CP) is a non-progressive movement disorder caused by damage to the developing brain, having an incidence of 3 out of 1000 newborn children (Germany et al. 2013; Robertson et al. 2017; Sigurdardottir et al. 2009). Cerebral palsy is in particular manifested through influences on motor development, although cognitive and perceptual problems are also prevalent (Rosenbaum et al. 2007). The severity of the brain lesion determines the degree of mobility (Graham et al. 2016).

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One major problem that can prevent normal physical activity in individuals with CP is that their muscles become gradually locked in inconvenient positions (so-called contractures) (Mathewson and Lieber 2015). Contractures in this case are defined as being increased muscle stiffness leading to decreased range of motion around joints without any active force production of the muscle (Pingel et al. 2017).

Contractures are therefore an important cause of reduced daily physical activity levels in CP subjects (Murphy 2010), resulting in a loss of strength, muscle atrophy, pain, and early onset fatigue (Barrett and Lichtwark 2010; Geertsen et al. 2015; Graham et al. 2016; Jahnsen et al. 2004).

It is also believed that there is a difference in fibre recruitment in CP subjects *versus* healthy controls (Stackhouse et al. 2005), which may further add to the muscle weakness they exhibit. Moreover, it has been found that there is an inherent stiffness in muscles of CP subjects, which can be significantly reduced following training (Willerslev-Olsen et al. 2014). As a form of suitable training, intensive gait training has been proposed as a beneficial means of preventing contractures in CP subjects (Willerslev-Olsen et al. 2014).

The aim of this study was to examine whether there is a difference in muscle fibre recruitment during treadmill exercise between CP subjects and healthy age-, sex- and BMI-matched controls.

The hypothesis tested was that CP subjects recruit muscle fibres in a less coordinated manner during periods of exercise compared with healthy controls.

This study is based on the above outlined problems and aims to revisit muscle functionality in CP subjects using the technique of acoustic myography (AMG). This technique enables a detailed and accurate measurement of muscles involved in a particular movement and is independent of electrical signals between the nerve and muscle, measuring solely muscle contractions, unlike surface electromyography (sEMG) (Harrison 2018). The AMG signal comprises three physiological parameters, namely efficiency/coordination (E-score), spatial summation (S-score) and temporal summation (T-score). This relatively new and portable technique of AMG shows considerable promise as a non-invasive method for assessing movement, movement type, muscle power and early fatigue status in most settings (Harrison 2018).

Materials and methods

Ethics

The study was carried out in accordance with the Helsinki Declaration and approved by the local ethical committee of the Capital Region of Denmark (H-15011541). All participants gave written, informed consent before participating in the study. Details from this study have already been published in part (Andersen et al. 2018).

Subjects

Twenty subjects were included in the present study [$n = 10$ adults with CP; and $n = 10$ healthy age-, sex-, and body mass index (BMI)-matched control subjects]. The CP group comprised 4 females (mean age = 42 years) and 6 males (mean age = 36 years). There were four hemiplegic patients in the CP group, and the data from the affected legs were included in the CP data set. The inclusion criteria were the following: all subjects with CP should have muscle contractures (Smith et al. 2011) in either the gastrocnemius or soleus muscle of one or both legs, and should at the same time be able to walk on a treadmill. The healthy control subjects were matched to the subjects with CP in terms of age, gender and BMI, and must not suffer from any skeletal muscle diseases or injuries, as well as being able to walk/run on a treadmill for 30 min. All subjects met the inclusion criteria. The contractures of the subjects with CP were, furthermore, clinically verified by measurements of range of motion and muscle volume (by circumference).

Additionally, the presence of muscle contractures was supported by the medical history of the subjects with CP, all of which had undergone treatment for contractures in their legs. Nine of the ten subjects with CP had undergone surgery for Achilles tendon extension, and all CP subjects had previously been diagnosed as being spastic by their general practitioner.

Experimental protocol

All subjects were instructed not to perform any physical exercise the day before the experiment and were asked to transport themselves to the study facilities without doing any physical activity such as walking or cycling. Furthermore, each subject rested for 30 min in a prone position upon arrival.

Acoustic myography

Acoustic myography (AMG) is a biomechanical method measuring generated pressure waves from a contracting muscle (Smith et al. 2011; Rose et al. 1994; Carlson 1974). AMG recordings were carried out with a CURO unit and CURO sensors (CURO-Diagnostics ApS, Denmark; formerly MyoDynamik ApS) and followed in real time on an iPADAir (Apple Inc, Cupertino, CA, USA) via the App "CURO Clinic" and a specialized data recording system. This allowed us to see the actual wave recordings and the ESTi score (E-, S- and T-score) while recording.

We used 50 mm sensors with a frequency recording range of 0.5–20 ± 0.5 kHz and the sampling rate was 4 kHz. Recorded data was stored to the CURO Unit and after completion of measurements transferred to the CURO software (https://app.myodynamik.com). The ESTi-score with its three components: (1) efficiency (E-score) (2) spatial fibre recruitment (S-score) and (3) temporal fibre recruitment (T-score), was calculated using the company software (Graham et al. 2016; Geertsen et al. 2015).

As an example, the S-score was determined as the signal amplitude in relation to a full 6 dB signal (measured as approx. 1 V). For more intuitive assessment of optimal muscle function, a scale of 0–10 was adopted, where 0 was considered as 0% optimal and 10 was considered 100% optimal. To calculate the score, the measured mV amplitude was subtracted from the maximal mV amplitude that could be accurately detected. The difference was then divided by the maximal amplitude and multiplied by 10 to yield a 0–10 scoring system. By way of an example, an S-score of 8 represents a signal with a very small amplitude (approx. 0.3 V), whereas an S-score of 1 represents a relatively large amplitude signal (approx. 0.7 V). The T- and E-score was calculated in a similar way to their full signal to give a score scale from 0 to 10, where 0 is full activity and 10 is no activity.

Musculus Gastrocnemius (lateral head) from both legs was measured. The ultrasound-gel coated sensor was placed centrally on the muscle body of each muscle (Contessa et al. 2016; Obst et al. 2017). Connecting cables were run from the sensors and connected to the CURO unit which was placed alongside the subject on a flat shelf attached to the treadmill. The wires from the sensors were secured with a flexible adhesive bandage and net stockings (Fig. 1).

Acute exercise

The exercise session included walking or running on a treadmill (Woodway PPS Med; Intra Medic AS, Denmark). The CP group participated in one session and the oral instruction was to walk or run as fast as they could for 30 min. One CP participant was only capable of walking for 10 min. The control group received the oral instruction to walk or run with the same speed and duration as their CP match.

During the exercise session, the subjective exhaustion level of each participant was assessed through a clinical VAS scale used as a Borg scale (Contessa et al. 2016). The exhaustion level was monitored at the following time points during the exercise session: 0 min, 10 min, 20 min, and 30 min. In addition, the heart rate was measured at the same time points using a heart rate monitor (Polar Electro ApS, Denmark).

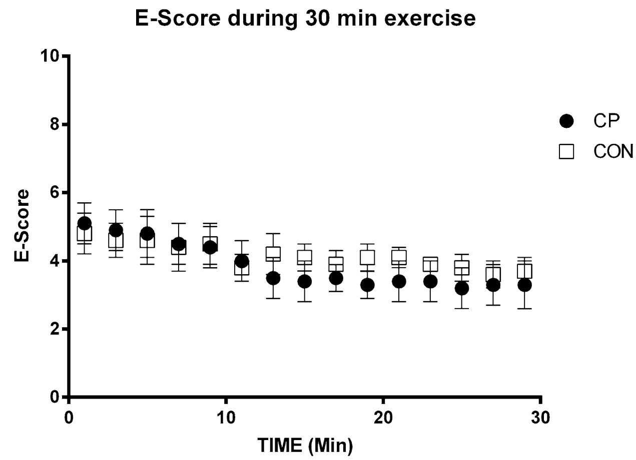

Fig. 1 The acoustic myography E-score from m. Gastrocnemius over time for the CP subjects (filled circle; n = 10) and healthy age, sex and BMI matched controls (open square; n = 10). Note that as the treadmill exercise progresses, the level of coordination and efficiency in the muscle signal from m. Gastrocnemius falls from an initial 5 to approximately 3. Values are presented as the mean ± SEM

Statistics

All statistics were performed using GraphPad InStat 3 for Mac (Version 3.0b, 2003; Graph-Pad Inc., La Jolla, CA). Data were initially tested for normal distribution and equal variance, and then subsequently analyzed using an unpaired *t* test. Differences between means with a P value > 0.05 were considered non-significant. Values are presented as the mean ± the standard error of the mean (SEM).

Results

Figures 1, 2 and 3 show the E- S- and T-scores respectively, for the CP and control subjects measured over the 30 min of physical exercise (walk/run).

The decrease in the E-score with time is indicative of a loss of coordination and efficiency with continued exercise and represents an impaired ability to switch "off" active fibres in between bouts of fibre activation (see Fig. 1). No significant difference was observed between CP and control subjects.

Interestingly, the S-score, reveals a significant difference between the CP subjects, who show a lower initial score, and controls, who had a higher initial score ($P < 0.01$ to $P < 0.05$). This finding indicates that the CP subjects have a higher degree of spatial summation to maintain the same speed of treadmill activity than the control subjects, i.e. they were recruiting significantly more fibres than the controls (see Fig. 2).

Finally, the T-score was a very similar pattern for both CP and control subjects (see Fig. 3). It reveals that over time,

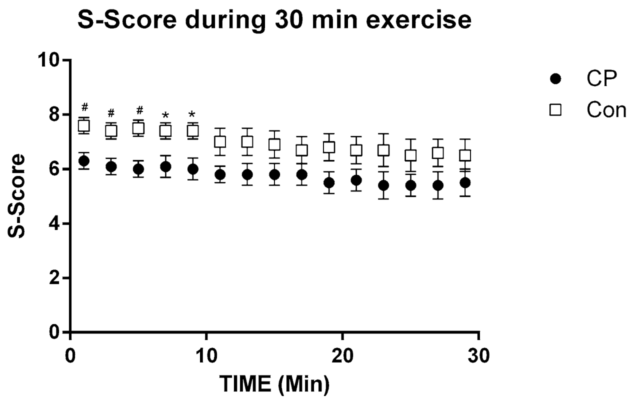

Fig. 2 The acoustic myography S-score from m. Gastrocnemius over time for the CP subjects (filled circle; n = 10) and healthy age, sex and BMI matched controls (open square; n = 10). Note the significant difference in the initial S-scores for the CP subjects *versus* the controls; #P < 0.01 and *P < 0.05. Values are the mean ± SEM

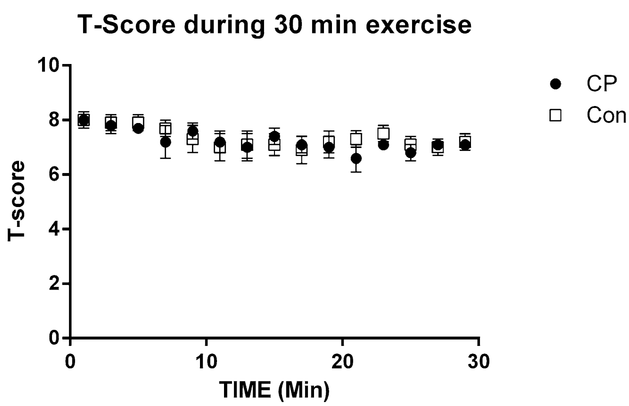

Fig. 3 The acoustic myography T-score from m. Gastrocnemius over time for the CP subjects (filled circle; n = 10) and healthy age, sex and BMI matched controls (open square; n = 10). Note that as the treadmill exercise progresses, the level of coordination and efficiency in the muscle signal from m. Gastrocnemius falls from an initial 5 to approximately 3. Values are the mean ± SEM

the T-score falls slightly, which is indicative of an increase in temporal summation—the subjects are over time on the treadmill firing active fibres at a faster rate (frequency). The initial T-score of 8.0 equates to a firing frequency of 51 Hz, and following 30 min of treadmill exercise the T-score of 7.1 equates to a firing frequency of 73 Hz.

Discussion

This study of 10 CP subjects and 10 healthy control subjects has revealed that in terms of the neural signalling for muscle control there is no real difference between the two groups. That is to say, CP and control subjects muscle function does not seem to differ in terms of its temporal summation (T-score) or surprisingly in terms of its level of coordination (E-score), over a 30-min period of treadmill physical activity, when matched to the same speed of control subjects.

Our hypothesis when initiating this study was that the CP subjects would recruit muscle fibres during a period of treadmill exercise in a less coordinated manner compared with matched healthy controls. This hypothesis can now be rejected, as Fig. 1 shows that the muscle coordination and efficiency (E-score) were found to be identical for both groups. This study has relied on the acoustic myography (AMG) technique to non-invasively measure muscle function (Harrison 2018). AMG comprises an evaluation of efficiency/coordination (E- score), as well as both spatial and temporal summation expressed by the S- and T-scores (CURO-Diagnostics ApS, Denmark; formerly MyoDynamik ApS), while the E score corresponds to the periods of active/inactive function relative to the duration of the activity period of the muscle (how long the muscle is "on"). In this way, measuring the relative period of muscle contraction to that of muscle relaxation during the treadmill exercise, it has been possible to assess any change in the level of muscle coordination both in a real-time and in minute to minute fashion.

The overall aim of this study has been to assess muscle fibre recruitment during treadmill exercise in CP subjects and healthy matched controls. It is clear from Fig. 2 that there is a recruitment difference between these two groups, at least initially when exercising on a treadmill. This difference, which was found to be significantly different for the first 9 min of exercise, affected the spatial summation parameter. In terms of recruitment, this means a higher number of fibres are recruited in CP muscles for any given muscle contraction. This was measured as being the amplitude of the recorded AMG signal, where larger amplitude gave a lower S-score.

The observation that the CP subjects have a lower S-score, which pertains to a greater degree of spatial summation, is most likely related to the fact that CP subjects generally have smaller muscle fibres than healthy age- and weight-matched controls (Rose et al. 1994). Thus, the lower S-score expresses a form of compensation for having smaller muscle fibres; more fibres are active to maintain the force needed to match the same speed as that of the controls. When producing muscle force, recruitment of fibres in a muscle happens either through recruiting many fibres at any given time, or by using fewer fibres fired at a higher frequency (Carlson 1974; Contessa et al. 2016).

It is well documented that CP subjects have less muscle mass, that their muscles are thinner and stiffer, and that they have a weaker force production in their muscles compared with matched controls (Barber et al. 2012; Barrett and Lichtwark 2010; Mathewson et al. 2014; Obst et al. 2017).

The findings of this study show, that in order to maintain the same treadmill speed as the controls, the CP subjects increased their spatial summation, whilst maintaining the same level of temporal summation and coordination as that of the controls (see Figs. 1, 2, 3). It should, however, be noted that the spatial summation difference between the CP subjects and the healthy controls was only significant for the first 9 min of exercise. Thereafter there was no significant difference for any of the parameters measured, although the healthy controls maintained a marginally higher S-score throughout the 30 min period.

It has been shown that there is an increase in the proportion of type I muscle fibres in some lower-extremity muscles in children with CP compared with unaffected children (Stackhouse et al. 2005).

This issue of muscle force and fibre size was raised in a recent paper focusing on AMG signals from women and men (Claudel et al. 2018). Here it was confirmed that the muscle force control between women and men was the same, despite a weaker 50% maximal voluntary force production in women compared with men (Claudel et al. 2018).

Another interesting finding from our study has been that the rate of fatigue appears to be very similar, if not identical at times, for CP subjects and healthy controls. In terms of the T-score, there was a similar rise in the firing rate of the muscle contractions (see Fig. 3) from 51 Hz at the start to 73 Hz at the end of the 30 min treadmill exercise. This serves to highlight that temporal summation for the CP subjects and the controls was identical under the conditions of exercise adopted in this study. However, we know that the CP subjects in this study did show other signs associated with fatigue (Andersen et al. 2018). For instance, it was observed that there was a significant difference ($P < 0.01$) in their Borg scales (exhaustion score from 0 to 10), with the CP subjects showing values at 10 min of 3.2, at 20 min of 4.3 and at 30 min of 6.3, compared with the controls; 0.2, 0.6, 0.9, respectively (Andersen et al. 2018). Combined, it can be concluded that with a similar firing frequency but an increased spatial summation, the CP subjects will be expected to fatigue ahead of the healthy controls, and in this respect the previously published Borg score differences concur.

In a recent study of voluntary muscle activation in children with CP it was concluded, that there is a need for a more detailed understanding of the mechanisms underlying muscle weakness in these subjects (Stackhouse et al. 2005). In agreement with Stackhouse et al. (2005), this study shows no signs of a difference in fatigability of the muscle itself between healthy controls and CP subjects over the 30 min period of treadmill exercise. However, it is clear from the blood lactate and the Borg scores that the two groups perceive the period of exercise differently. With relatively more type I fibres, and muscle fibres of a smaller cross-sectional area in general, one can expect a weaker force production in the CP subjects compared to healthy controls. However, this study and its findings tend to dispel the hypothesis raised by Stackhouse and colleagues that "..ambulatory children with spastic diplegia may use the same motor units more repetitively and for longer durations..". Neither the T- or E-scores recorded here support this. In contrast to another statement by Stackhouse and colleagues ".. the lower force-generating capacity in children with CP creates a lower force reserve to sustain activity..", our results do not agree, as the S-score data illustrate that the CP subjects with their smaller and weaker fibres rely on spatial summation to try to match the treadmill exercise level of healthy controls.

Conclusions

In conclusion both the CP and control group control and regulate muscle contractions in an identical fashion. However, the maximal pace achievable by the CP subjects was always lower than that possible by healthy controls. One possible explanation for this exhibited weakness in CP subjects could be related to their documented smaller muscle mass and altered fibre type proportions compared with those of healthy controls. Findings of a significant difference between CP subjects in terms of their Borg score over the 30 min of treadmill exercise, despite similar AMG data from m. Gastrocnemius, now raises the issue of peripheral *versus* central fatigue aspects in this disease. Further studies are warranted to fully understand the metabolic and morphological properties of the muscles of CP subjects, as well as AMG studies comparing upper and lower extremity muscle function, so as to reveal the mechanisms underlying their muscle weakness.

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Compliance with ethical standards

Conflict of interest All the authors declare that they have no conflict of interest in the present study.

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