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ADVANCES IN PEDIATRIC RESEARCH

Intensive gait training in toddlers with cerebral palsy: A pilot study

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Abstract

Background: Reduced muscle growth may be involved in the development of contractures in children with cerebral palsy (CP). Here, we report data from a pilot study of intensive gait training in CP toddlers.

Methods: Five children with CP aged 8-30 months performed activity-based gait training for one hour/day, five days/week for three consecutive months. Included children were diagnosed with spastic CP, had a Gross Motor Function Classification System (GMFCS) score of I–II, and were not epileptic. All children wore pedometers during training. Before and after the training period, kinematic and qualitative gait analysis, clinical and objective evaluation of spasticity, Gross Motor Function Measure-66 (GMFM-66), and ultrasound of the affected medial gastrocnemius (MG) muscle were performed. Two children were also tested before and after three months of receiving only standard care (SC).

Results: On average 1410 steps/session were logged during 63 days of training. More steps were achieved at home than at a central facility. During training, MG muscle volume increased significantly, while it decreased for SC children. Gait improved qualitatively in all children, and GMFM-66 score improved in four of the five children. Similar improvements were seen among the SC children. Two children had pathologically increased muscle stiffness prior to training, which was reduced during training. Reflex stiffness was unchanged in all five children.

Conclusions: This pilot study suggests that intensive gait training may increase muscle volume, improve walking skills and reduce passive muscle stiffness in toddlers with CP.

Citation: Herskind A, Willerslev-Olsen M, Ritterband-Rosenbaum A, Zacho Greve L, Lorentzen J, Nielsen JB (2016) Intensive gait training in toddlers with cerebral palsy: A pilot study. Adv Pediatr Res 3:8. doi:10.12715/apr.2016.3.8

Received: April 23, 2015; Accepted: September 30, 2015; Published: July 1, 2016

Competing interests: The authors have declared that no competing interests exist.

Sources of funding: This study was made possible thanks to generous financial support from The Ludvig and Sara Elsass Foundation.

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Introduction

Cerebral palsy (CP) is caused by an injury to the developing brain and is the most common motor disability in childhood [1-3]. CP restricts children's everyday activities and reduces their daily level of activity [4, 5]. More than 50% of a large cohort of children with CP was found to have limited or no independent walking skills [6]. Muscle contractures are one of the main physical problems for children with CP [7]; these develop in the ankle joint before three years of age [8, 9]. Contractures inhibit joint range of motion and may lead to joint deformities [7]. The pathogenesis of contractures is not yet fully understood, but impaired muscle growth is thought to be a key element [10].

Muscle growth in early childhood is determined by genetic factors as well as nutrition, metabolism and neural activity [11, 12]. Use and disuse of the muscles determine the activity of several signalling factors involved in regulating protein synthesis and degradation, and which determine the overall rate of muscle growth [13, 14].

We recently showed that 15-month-old children with CP have a significantly reduced medial gastrocnemius (MG) muscle volume compared to typically developing (TD) children, which was unrelated to differences in overall growth between the two populations [15]. Furthermore, more severely affected children showed the largest reduction in muscle [15]. This suggests that reduced physical activity and neural activation of the muscle in children with CP before 15 months of age may be responsible for muscle atrophy. If so, it is crucial to ensure development of the motor skills required for children with CP to become physically active early in life to avoid atrophy and loss of function.

Furthermore, the young brain appears to be more plastic and thus more susceptible to intervention than the adult brain [16, 17]. Kitten studies have shown evidence of so-called 'critical periods' during development in which the corticospinal tract fine-tunes its functional connections with spinal motoneurones, and during which motor training may effectively improve functional capacity [18, 19]. It remains unclear as to what extent similar critical or sensitive periods exist during human development, but several studies imply that the first years of development may constitute a window of opportunity [17].

Yang and co-workers [20] suggest that gait training in toddlers with an early brain lesion may positively affect functional ability and cause plastic changes in the corticospinal pathway. We hypothesized that gait training would also increase their daily level of activity, thus preventing muscle atrophy and possibly the development of contractures. Long-term follow-up is required to determine the effect of such an intervention. Here we present data from a pilot study to determine the feasibility of a longer-term study on the use of gait training to increase muscle volume and decrease muscle stiffness in toddlers with CP .

Methods

The following protocol was approved by the local ethics committee, Region H. Trial registration number: H-1-2014-006, Ethical Committee of Region H (De Videnskabsetiske Komiteer for Region Hovedstaden).

Participants

Five toddlers (mean age 18 months; range 14–26 months; four boys) participated in the pilot study. Children were included if they were 8–30 months old (corrected age; CA), diagnosed with spastic CP, had a Gross Motor Function Measure Score (GMFCS) of I–II, and did not suffer from epilepsy. Two children (P2; P5) were born preterm, thus their corrected ages were used. Two of the five children (P1; P5) walked independently at the beginning of the training period. Two could take a limited number of steps (P3; P4), and one had not yet learnt to walk (P2). One child (P2) had received one botulinum toxin A (BoNT-A) treatment in the triceps surae muscle group prior to enrolment. None had received leg surgery. Characteristics of all children are shown in Table 1. Concurrent with the training, all children received standard care (SC consisting of regular visits to a paediatrician, physiotherapist and occupational therapist according to the child's needs.. Additionally, seven TD children (mean age 16 months; range 6–24 months; five boys) were measured for passive muscle stiffness and reflex stiffness. All parents provided written consent for their children to participate in the study.

All children were tested before and after the intervention. Two of the children (P4; P5) in the intervention group took part in three months of SC before the intervention started. They were tested before and after this period of SC.

Table 1. Participant characteristics

Participant	Sex (M/F)	Age at start of training (mo)	No. of sessions	GMFCS level	Hemi-/diparesis (H/D)	Independent walker at start of training (Y/N)	Previous leg surgery (Y/N)	Previous BoNT-A treatment (Y/N)
P1	M	14	60	I	H	Y	N	N
P2	M	26 CA	66	II	D	N	N	Y
P3	F	15	59	II	D	N	N	N
P4	M	24	63	I	H	N	N	N
P5	M	20 CA	65	I	H	Y	N	N
Mean (SD)		20 (5.0)	63 (2.7)					

SD: standard deviation; M: male; F: female; CA: corrected age; GMFCS: Gross Motor Function Classification Score; H: hemiparesis; D: diparesis; BoNT-A: Botulinum Toxin A

Intervention

The intervention consisted of daily, intensive gait training for 1 hour/day, 5 days/week for three consecutive months; training usually took place at a central facility, the Helene Elsass Center (www.elsasscenter.dk). Each child received individual training sessions with a staff member and a parent present. Training focused on muscle strength in the legs and trunk, and balance. Exercises included supported walking on a treadmill with 10% incline, walking up and down several flights of stairs and in hilly terrain, walking on even and uneven surfaces and using a cart, and running. All exercises were performed both with and without a 500 g load around each ankle during most or all of the session. Exercise difficulty increased with skill. All children were video-recorded regularly during training sessions.

The first three children all received their training at the centre, with occasional home-based training because of holidays or staff illness. The next two children trained at the centre 5 days/week for the first 2 weeks; the next 2 weeks they had 4 days/week of training at the centre and 1 day at home, then one month of training for 3 days/week at the centre and 2 days at home. In the last month they came to the Helene Elsass Centre for 2 days/week and trained 3 days/week at home. Parents of all children were given written and oral instructions on how to perform the training at home .

Pedometer recordings

Previous studies have show that the use of pedometers has high reliability and validity in populations of children both with and without CP [21, 22]; hence all children in our study wore a pedometer (Fitbit Flex, USA) during each training session. The pedometer was placed around the ankle and set to the most sensitive settings. The child also wore the pedometer during training sessions at home or when on holiday. Data were regularly transferred from the pedometer to a PC via a wireless connection, and an average number of steps was calculated for each child.

Neurological examination

At the beginning of each test session, all children were examined by either a medical doctor (JBN) or a physical therapist (JL) with several years of experience of neurological examinations in children. Tests were performed when the child was as relaxed as possible. Passive range of motion (ROM) of the ankle was evaluated by slowly moving the foot as far in the plantar and dorsal directions as possible. Any resistance during the movement was noted. From a neutral position, the ankle joint was then examined by fast, passive dorsiflexion of the foot to evaluate whether catch and/or clonus were present. Similar movements were applied with the joint in a more dorsi-flexed or plantar-flexed position to evaluate a score on the Modified Ashworth Scale (MAS). The patellar and Achilles tendon reflexes were tested, and

voluntary muscle force in ankle plantar-flexion and dorsiflexion, knee flexion and extension, and hip flexion was assessed.

Qualitative evaluation of walking skills

To evaluate the development of walking skills during the training period we used the Edinburgh Visual Gait Score (EVGS), which was recently validated for use in children with CP [23]. The EVGS consists of 17 different items and assesses the ankle, knee, hip, pelvis and trunk during stance and swing phases [24]. However, we only used it as a guideline, since this scale was developed using children with CP aged 9–15 years and not toddlers.

Gross motor function

An experienced physical or occupational therapist, who were not involved in the training sessions, tested children's gross motor function using The Gross Motor Function Measure-66 (GMFM-66).

Gait kinematics

Gait pattern was analysed while the child walked on a treadmill using a 3D motion-capture system (Qualisys, Gothenburg, Sweden); children unable to walk independently were supported with a hand-rail. The most comfortable treadmill walking speed for each child was chosen during the first test session. In following sessions, speed was initially set to that decided in the first test and then increased according to the child's ability. Children walked in their own shoes – none used inserts or braces – and they walked on the treadmill for at least 1 minute. Three-dimensional kinematic data was captured using six synchronous Oqus 1 cameras operating at a sampling frequency of 200 Hz. Each child wore 12 mm reflective markers, bilaterally at the lateral articular line of the knees, the lateral malleolus and the lateral side of the fifth metatarsal.

Ultrasound

Researchers trained in the use of ultrasound (US) examined the entire length of the MG muscle to assess muscle volume. Height, weight, circumference of the widest part of the crus, leg length and fibula length were measured. US was performed on the leg most affected by CP, with the child's ankle fixed in a neutral angle. One image was recorded with the probe positioned longitudinally at the mid-belly of the MG to estimate muscle thickness and fascicle length. Several images were recorded with the probe aligned transversally along the length of the muscle at 10 mm intervals to create a 3D reconstruction of the MG. The probe was hand-held and fixed vertically with the lower leg for all images. A modified, free-hand, 3D US technique was used to measure muscle volume and length. For further details see Herskind et al. [15] and Barber et al. [25].

Evaluation of passive stiffness and reflex stiffness

Passive and reflex-mediated stiffness of the ankle plantar-flexors were objectively assessed according to the methods described in Lorentzen et al. [26] and Willerslev-Olsen et al [8]. With the child seated comfortably, the most affected foot was attached to a rotating footplate delivering maintained torques up to 80 nm and peak torques up to 120 nm. Ankle joint angle and torque exerted on the foot plate were measured prior to and during the stretch perturbations, which consisted of ramp and hold dorsi-flexion with a 6° amplitude at 17 different velocities between 5 and 220°/s. Perturbations were delivered in a random order every second; up to 10 trials per velocity were collected. Bipolar EMG recordings were obtained from two sets of electrodes placed over the soleus muscle and the tibialis anterior muscle belly. Passive stiffness was calculated from the torque response at low velocities without stretch responses. Reflex stiffness was calculated from the additional torque response to the fastest perturbation.

Results

Pedometer recordings

During the 3 months of training for 1 hour/day, five days/week, each of the five children performed a mean of 63 days of training (range 59–66 days) and the pedometers logged a mean of 1,410 steps/session for each child (range 989–2,087 steps). The three

children who had all of their training at the Helene Elsass Centre logged a mean of 1,066 steps/session per child at the centre and 2,051 steps/session per child when training at home. The two children who performed an increasing amount of the training at home logged a mean of 1,165 steps each when training at the Helene Elsass Centre, whereas they logged a mean of 2,461 steps/session each while performing the training at home.

Neurological examination

Details of neurological examinations are given in Table 2. All children except for one (P1) showed some degree of increased muscle tone, as evaluated by the MAS. Except for one child on a single occasion (P2), the children showed no signs of reflex hyperexcitability, and none had clonus or catch at any time. One child (P2) had an increase in MAS and another child (P5) had a decrease after the training period. One child's (P2) ROM was reduced and another child (P4) had improved ankle ROM after the training period.

Qualitative evaluation of walking skills

Gait was analysed using the EVGS as a guideline. After the 3 months of training, P1 showed improved ankle dorsiflexion on the affected side during both swing and stance phases, and increased outward rotation in the hip of the affected leg had disappeared. P2 crossed his legs more during walking and there was a bilateral increase in toe-walking. P3 showed improved outward rotation in the hip, knee and foot on the affected side. There were no visible changes in P4's walking skills. P5 showed increased muscle strength in the affected leg and reduced hyperextension of the knee during stance.

Table 2. Clinical evaluation of spasticity

Participant	P1		P2		P3		P4		P5	
	R	L	R	L	R	L	R	L	R	L
Pre-control										
Patellar	-	-	-	-	-	-	2	1	0	0
Achilles	-	-	-	-	-	-	1	0	1	0
MAS	-	-	-	-	-	-	3	0	3	0
Ankle ROM	-	-	-	-	-	-	0° df	F	F	F
Clonus	-	-	-	-	-	-	÷	÷	÷	÷
Pre-training										
Patellar	1	0	1	1	-	-	1	1	1	1
Achilles	1	0	0	0	-	-	0	0	0	0
MAS	0	0	3	2	-	-	3	2	1	0
Ankle ROM	F	F	F	F	-	-	0° df	F	F	F
Clonus	÷	÷	÷	÷	-	-	÷	÷	÷	÷
Post-training										
Patellar	1	1	1	1	1	1	1	1	0	1
Achilles	1	1	0	0	0	0	0	1	0	1
MAS	0	0	4	4	0	0	3	0	0	0
Ankle ROM	F	F	15° df	15° df	F	F	10° df	F	F	F
Clonus	÷	÷	÷	÷	÷	÷	÷	÷	÷	÷

Patellar: Patellar reflex; Achilles: Achilles reflex; MAS: Modified Ashworth Scale; ROM: Range of motion; R: right; L: left; F: Full; df: dorsi-flexion. Ankle ROM indicated in relation to anatomic position

Gross motor function

As recommended by Yang et al. [20], we compared the change in children's total GMFM-66 scores and their Dimension D (standing) and E (walking and running) scores, respectively, to the minimum change scores needed to gain a Minimum Clinically Important Difference (MCID) estimated for children aged 4 years or older [27]. For the total GMFM-66 score, four children (P1–3; P5) improved beyond a large effect size after the training. P4's total score was not improved. Both of the children in the control group improved beyond a large effect size. In GMFM Dimension D, P5 improved to a large effect size and two children (P1; P3) improved to a medium effect size after the training. P2's improvement was insignificant, and P4's score declined. In the control group, both children improved beyond a large effect size. For Dimension E, three children (P1; P3; P5) made large improvements, P4 improved to a medium effect size and P2's improvement was insignificant after the training. During the control period, both children made large improvements.

Gait kinematics

Prior to training none of the children could walk on the treadmill for more than 90 seconds. After training, children walked for at least 120 seconds, and all performed several tests at different walking speeds within the same session. The comfortable gait speed on the treadmill varied between 0.5 and 1.1 km/h at the preliminary tests, and between 0.6 and 2.2 km/h after the training. Prior to training, none of the children showed any heel strike during walking, but had flatfoot contact with the ground without toe lift. After training, the four children (P3 did not complete the final gait kinematics test) showed heel strike with toe lift prior to ground contact in at least some steps (Figure 1A; average: 31% of steps; mean amplitude of toe lift: 32 mm). Consequently, the ankle joint was in a more dorsi-flexed position at the time of heel strike following training (Figure 1B). Ankle joint ROM during the gait cycle increased in three of the children (P1; P3; P4), whereas a decrease was seen in one child (P5) (Figure 1C).

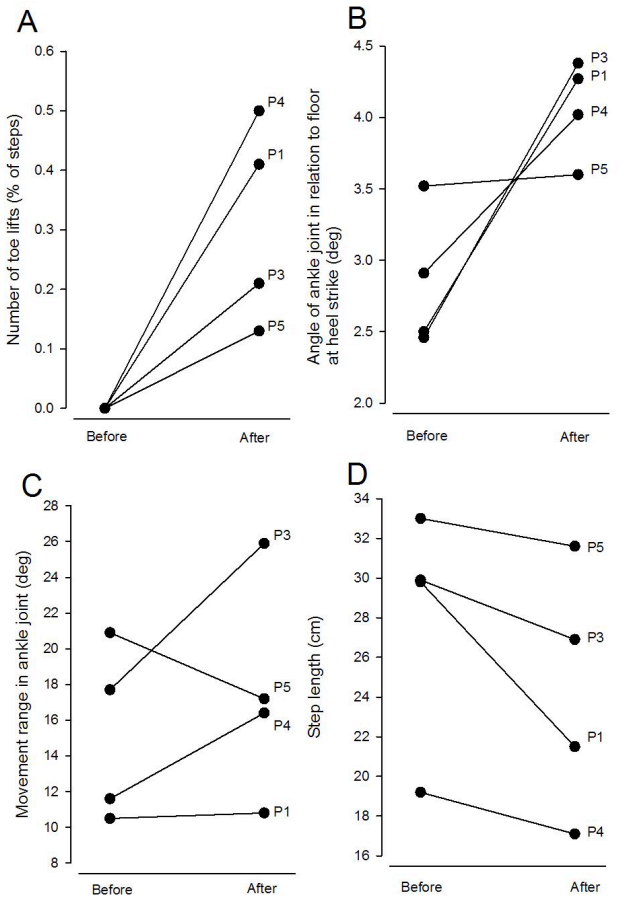

Figure 1. Kinematics of treadmill walking. Number of toe lifts (A), angle of ankle joint at heel strike (B), and ankle range of movement (C) for each of the children before and after the 3 months of training. P2 did not complete the final gait kinematics test.

Ultrasound measures

MG volume and thickness increased significantly in all children following training (Figure 2A; $p < 0.01$), whereas a decrease was observed for the two children during the control period (Figure 2B). Prior to training, the average muscle volume was 13.9 ml; 7 ml (33%) less than age-matched TD children [15]. After training, the average muscle volume had increased to 20.1 ml, which was only 3 ml (13%) less than TD children. Fascicle length and pennation angle showed a small increase after training (fascicle length: 24.9 and 27.9 mm, before and after training, respectively; pennation angle: 16.3° and 19° before and after training, respectively).

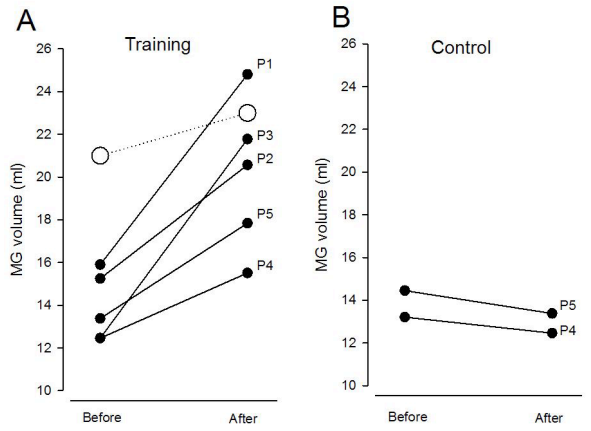

Figure 2. Ultrasound measures of medial gastrocnemius muscle volume. Increment in medial gastrocnemius (MG) muscle volume (A). Full black circles represent each of the children (P1–5) before and after the 3 months of training. The dotted black line shows the development of MG muscle volume in age-matched TD children. (B) Shows changes in MG volume for the two children in the control group after 3 months of standard care.

Passive muscle stiffness and reflex stiffness

Passive muscle stiffness varied considerably, ranging from 10 to 40% of T_{max} in the TD children with no clear age-dependency (Figure 3A; black circles). Measurements from the seven, age-matched TD children are shown in the figure. Passive muscle stiffness in CP children was high in the normal range in three cases (P1–3) and above the normal range in two cases (P4; P5) prior to training (Figure 3A). During the control period, passive muscle stiffness increased in both children (Figure 3A; compare open squares and open triangles) and was reduced during the training period in both (Figure 3A; compare open triangles and closed triangles). There was either no change or a small increase in passive muscle stiffness in the three other children. Notably, the two children (P4; P5) with reduced stiffness after training also showed the highest stiffness prior to training.

With the fastest stretch (200°/s; 6° amplitude), stretch reflexes could be determined in the soleus EMG in all TD and CP children, with an average latency around 40 ms. Among the TD children, the average reflex elicited torque was 26 ± 4.5% of T_{max} ranging from 5 to 50 with no clear age-dependency. Reflex-mediated torque was within this range in all the children with CP except one (P2). After training, reflex stiffness increased in three children (P2; P3; P5), remained unchanged in one (P4) and decreased in the last child (P1; Figure 3B; compare open triangles and closed triangles). Reflex stiffness decreased slightly during the control period in both children (Figure 3B; compare open squares and open triangles).

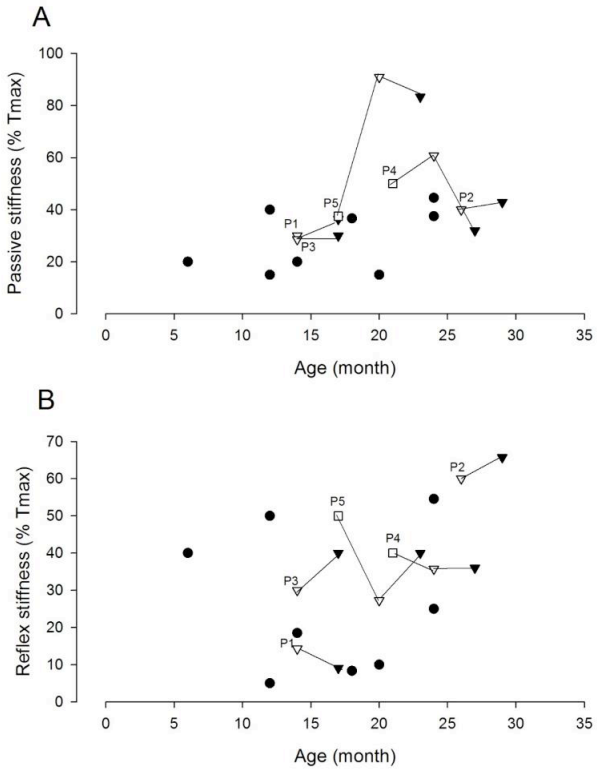

Figure 3. Reflex mediated stiffness and passive muscle stiffness. Changes in passive muscle stiffness (A) and reflex mediated stiffness (B) before and after training. Open triangles represent testing pre-training; black triangles post-training. For P4 and P5, the open squares represent testing prior to inclusion in the control group. Black circles show measurements from age-matched TD children.

Discussion

Increased muscle volume and measurements of muscle stiffness

The goal of the intensive gait training studied here was not for children to become independent walkers, rather to improve their level of activity to prevent atrophy of the leg muscles and thereby avoid contractures. All children increased their MG muscle

volume significantly after 3 months of training, whereas muscle volume for the children in the control group decreased. Despite the small number of children included in this study, the results indicate that an intensive program of physical activity may effectively stimulate muscle growth in CP children, in whom muscle growth otherwise appears to stagnate at around 15 months of age [15, 25]. If current ideas about the relationship between muscle growth and contracture development [10] are correct, then intensive physical activity similar to that performed in this study may help to prevent contractures.

We were unable to demonstrate a clear effect of training on children's ankle muscle stiffness, since we observed instances of no change and decrease. This might be partly related to the small number of children and the high variability of the measures [8], but it is also likely that some of the children had not yet developed, or would never develop, alterations in the passive elastic properties of their muscle and connective tissues. This type of training is unlikely to have any measurable effect if the elasticity of the tissue is within normal range prior to training [8]. It is therefore noteworthy that, in two children (P4; P5), passive muscle stiffness was reduced after training, when their passive stiffness had been above the range of TD children prior to training. These two children also showed improved ROM in the neurological examination. The fact that both children in the control group increased their passive stiffness further strengthens the idea that training may counteract the processes leading to increased muscle stiffness, and eventually clinically manifest as contractures.

The small number of children in this pilot study prevents us from making conclusions with any real certainty. The fact that this is is the first study to attempt measurement of muscle stiffness with instrumented, computer-controlled biomechanical and electrophysiological techniques in toddlers provides an additional reason to be cautious because this method has not yet been validated in this population. We were thus forced to extrapolate from previous findings in a 3-15 year old age group [8], but there are several reasons why this may be problematic. For example, the small feet and low masses of the children in our pilot posed technical challenges requiring significant equipment alterations. The smallest children's feet were only slightly larger than the diameter of the axis of the foot plate, and leg mass was generally lower than the mass of the foot plate. Both factors challenge an exact measurement of the resistance to the imposed movement. Relating the measurements to the maximal torque evoked by electrical stimulation of the tibial nerve in the individual child partly solves these problems, but it remains that the small torques involved are very sensitive to small differences in measurement conditions. Thus, the measurements are much more variable than have been seen in older children. In two of the children (P2; P4) measurements could not be obtained without some background EMG activity prior to the stretches. In these cases it is difficult to decide whether the cause was the child being unable to relax because of spastic dystonia, or whether the child was simply non-cooperative. Further studies in a larger population of TD and CP children are clearly necessary to clarify such issues. Nevertheless, the current study provides evidence that it is feasible to obtain these measures even in very small children.

Improvements in gait ability and gross motor function

Two children (P3; P4) learnt to walk independently during the training, but it is impossible to determine whether this was because of the training. All children showed larger toe lift and a more dorsiflexed ankle joint at ground contact during treadmill walking, suggesting that training may have benefitted the development of a gait pattern more similar to TD children. Similar improvements were also observed during over-ground walking. Two children (P1; P3) showed less outward rotation in the leg and one showed clear improvement in toe lift, also during over-ground walking. The three remaining children, who were also the most severely affected by CP, showed no visible changes and continued to make ground contact with either the front of the foot or the entire foot. These modest effects may partly be caused by a lack of a standardized and validated scoring system for gait in toddlers. We attempted to adapt the EVGS [24], but it is not optimal for scoring toddlers' emergent gait, and it may be questioned if scoring the variable and quickly developing gait in toddlers is feasible. Given the importance of identifying pathological gait at an early age, a valid

scoring system for toddler gait would, however, be valuable.

Four of the five children greatly improved their total GMFM-66 score after the training period, three improved their standing, and four their walking abilities. However, both children in the control group made similar, large improvements, so in this small sample it is difficult to distinguish the children's normal development from progress made during the training.

Is daily training in this population feasible?

It was possible to keeping the children motivated for the entire training period by making the training sessions fun and challenging for each child. The child's parent usually played an active part in the training sessions, which encouraged the child. All children logged more steps during their training sessions at home than at the Helene Elsass Centre. After noting this result in the first, three children (P1–3), who had the majority of their training at the centre, the next two children (P4; P5) had more training sessions at home, where they logged even more steps. However, P4 and P5 were both classified as GMFCS I, whereas in the first group only P1 were GMFCS I, and P2 and P3 equalled GMFCS level II, which may have influenced the total number of logged steps. Either way, the increased number of steps at home is promising, since a training protocol as intensive as this one requires ample health care resources. A combination of periods of therapeutic-supervised and parent-supervised training could be an effective and less costly way to train children.

Conclusions

This pilot study shows that it is feasible to considerably increase the daily activity level of children with CP aged 14–26 months (CA) and thereby facilitate growth of their ankle muscles. The study also demonstrates the feasibility of measuring passive muscle stiffness in this population. Longitudinal studies are necessary to demonstrate whether an increased level of physical activity also diminishes risk of developing muscle contractures.

Acknowledgements

We are very grateful to the parents and children who participated in this study for all their enthusiasm and patience. We would like to thank Helle Hüche Larsen and Jonas Skafte Jensen for testing the children's gross motor function, and the Helene Elsass Centre staff, who supplied the children with fruit.

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