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FACULTEIT GENEESKUNDE EN LEVENSWETENSCHAPPEN
master in de revalidatiewetenschappen en de kinesitherapie

Masterproef

Muscle fatigue during isometric grip tasks in adolescents with unilateral cerebral palsy

Promotor :
Prof. dr. Katrijn KLINGELS

Copromotor :
Mevrouw Deborah SEVERIJNS

Kendra De Koninck
Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie

universiteit hasselt
KNOWLEDGE IN ACTION

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Ondermeel 6, 3990, Peer, Belgium, 19 May 2015 K.D.K.

Research context

Cerebral Palsy (CP) is the most common motor disorder in children (1). It is important to understand the pathophysiology and the symptoms of this pathology for an optimal treatment. A common complaint in this population is fatigue, and more specifically physical fatigue (2). Physical fatigue can be objectified by the measurement of muscle fatigue (3). However, there are only a few studies published about muscle fatigue in this population. Most of these published articles describe muscle fatigue in the lower limbs and the results are inconclusive. Therefore, the aim of this master thesis is to gain insight in muscle fatigue in adolescents with unilateral CP in the upper limbs and more specifically: to investigate if there is a difference in muscle fatigue between both hands in adolescents with unilateral CP and compare muscle fatigue in both hands between adolescents with unilateral CP and healthy adolescents. These insights may help in optimizing treatment interventions.

This experiment is situated in the research field of the paediatric rehabilitation. This pilot study fits in a broader framework of the PhD project of Dra. D. Severijns, entitled “Motor fatigue during upper and lower extremity function in Multiple Sclerosis”.

The design of the experiment was already drafted by Dr. E. Rameckers. He also tested the adolescents with CP. Typically developing (TD) adolescents were recruited and tested by myself in the Don Bosco college, Hechtel-Eksel, Belgium.

The data from the experiment was converted to usable data for statistical analysis by myself with a custom-made program written by Dra. Severijns. Thereafter I performed the statistical analysis and wrote this article. Prof. K. Klingels and Dra. D. Severijns performed the proofreading.

1. Surveillance of Cerebral Palsy in E. Surveillance of cerebral palsy in Europe: a collaboration of cerebral palsy surveys and registers. Surveillance of Cerebral Palsy in Europe (SCPE). Developmental medicine and child neurology. 2000;42(12):816-24.
2. Jahnsen R, Villien L, Stanghelle JK, Holm I. Fatigue in adults with cerebral palsy in Norway compared with the general population. Developmental medicine and child neurology. 2003;45(5):296-303.
3. Bigland-Ritchie B, Johansson R, Lippold OC, Woods JJ. Contractile speed and EMG changes during fatigue of sustained maximal voluntary contractions. Journal of neurophysiology. 1983;50(1):313-24.

Muscle fatigue during isometric grip tasks in adolescents with unilateral cerebral palsy

AIM To evaluate muscle fatigue during a sustained grip contraction in the upper limb in adolescents with unilateral cerebral palsy (CP) compared with typically developing (TD) adolescents.

METHOD Twenty-three adolescents with CP (11 males, 12 females; mean age 14y, SD 1.43y, range 11-17y; Manual Ability Classification Scale levels 1-3) and 23 sex and age matched TD adolescents participated. Muscle strength and muscle fatigue during a 30 seconds maximal isometric contraction were measured in both hands in two grip positions: hand grip and pinch grip. Muscle fatigue was analysed with the static fatigue index (SFI). Anthropometric variables were weight, length and hand length.

RESULTS For both grips the SFI was significantly higher for the CP group compared with the TD group in the affected and in the non-affected hand ($p<0.0001$ for each comparison). For the pinch grip the SFI of the affected hand of the CP group was significantly higher compared with the SFI of the non-affected hand ($p=0.02$). Only in the TD group there were correlations between SFI and age, weight and hand length.

INTERPRETATION Adolescents with CP show more muscle fatigue compared with TD adolescents during a 30s maximal isometric hand grip task and a pinch grip task.

What this paper adds:

- CP adolescents have higher muscle fatigue, shown by the SFI
- There were no correlations between SFI and anthropometric CP data
- There was no correlation between strength and SFI in CP
- There was a correlation between non-affected grip strength and weight
- Pinch grip strength was correlated with length in CP adolescents

Short title: Muscle fatigue in children with CP

Cerebral palsy (CP) is an umbrella term describing a group of disorders of movement and posture, causing activity limitation, which are caused by a non-progressive lesion that occurred in the developing fetal or infant brain.[1] CP has an incidence of two to three per 1000 live births and is the most common cause of motor problems in young children.[2] Common motor problems are abnormal muscle tone, muscle weakness and coordination problems.[1] The motor disorders of CP are often accompanied by disturbances of sensation, cognition, communication, perception, and/or behaviour.[1] Fatigue is another complaint often reported in children with CP.[3]

There is no exact definition of fatigue.[4] Fatigue consists of a neurophysiological component, a neuropsychological component and a subjective sensation.[5] Neurophysiological fatigue is the failure of the system to sustain force or power output, while neuropsychological fatigue is the failure of the system to sustain a mental task.[5] Both components can be measured objectively.[5]
Kluger et al. [6] defined objectively measured fatigue as fatigability.[6] Neurophysiological fatigue can be objectified by the measurement of muscle fatigue, which is the reduction of force of the neuromuscular system during a sustained task.[7] Neuropsychological fatigue can be measured as a decline in reaction time or accuracy over time in continuous performance tasks or in a probe task given before and immediately after a fatiguing cognitive task.[6]

Both peripheral (muscle) and central factors (central nervous system and nerves) induce muscle fatigue.[8] Several assessment methods for muscle fatigue have already been documented in other populations. It has been stated that in children with CP muscle fatigue can be measured for example by using EMG-measurements or by using the time that a force can be held.[9] For EMG-measurement, fatigue parameters are the median/mean frequency of the force density spectrum of the EMG and the root mean square of the EMG-amplitude.[10] For the analysis of muscle fatigue during a muscle contraction in a pre-defined timespan different methods and outcome measures exist: for example the static fatigue index, which is based on the area under the force-time curve.[11,12]

So far only a few studies have investigated muscle fatigue in children with CP. Moreover, most research focused on muscle fatigue in the lower limbs. Previous studies showed no difference in endurance time between children with spastic CP and typically developing (TD) children during an isometric knee-extension at 50% of the maximal force till 5% drop.[13,9,14] However, a difference was found in EMG outcomes with lower median frequency of the vastus lateralis muscle and rectus femoris muscle, normalised by the initial value in children with CP compared to TD children. A lower normalised median frequency points to higher muscle fatigue because of abnormal muscle function.[9] Furthermore, the EMG root mean square of the vastus lateralis muscle and the rectus femoris muscle was significantly higher in the control group compared with the affected leg of the CP group.[9] Therefore, Leunkeu et al. [9] concluded that children with CP were unable to recruit higher threshold motor units or to drive lower threshold motor units to higher firing rates. There was also a steeper slope of the EMG-median frequency in the affected leg of the CP group compared to the non-affected leg and compared to TD children indicating that children with CP experienced more muscle fatigue in the affected leg.[9] In contrast, another study showed that during an isokinetic knee-extension and -

flexion protocol the affected leg of the CP group was less or equally fatigued than the TD children based on the peak torque and the EMG median frequency.[15-17]

In children with CP the upper limbs can also be affected causing problems during eating and personal care.[18] In daily life, maximal strength in the upper limbs is important. The maximal grip strength of the non-dominant hand of children with CP has shown to be correlated with manual ability.[19] However, in daily activities, such as drinking a cup of tea or eating, not only the maximal strength is important but also the ability to sustain a contraction for longer periods, defined as muscle endurance. So far, only two studies have been published on muscle fatigue in the upper limb in children and young adults with CP and results are inconclusive.[20,21] A first study examined isometric hand grip muscle fatigue in young adults with unilateral CP (mean age 21.2 years).[20] In this study, the patients were asked to squeeze as hard as possible with their hand during 20 seconds. Muscle fatigue was analysed with the static fatigue index, which is based on the time-strength curve where the area under the curve is compared with the hypothetical area under the curve without strength loss.[11,12] Interestingly, no difference was reported in muscle fatigue between the affected and non-affected side in young adults with unilateral CP. Results also showed that young adults with unilateral CP had more muscle fatigue compared to healthy young adults.[20] On the contrary, the second study reported that there was no difference in endurance time and EMG median frequency slope between adolescents with unilateral CP (mean age 12.3y) and TD adolescents during an isometric elbow flexion on a low force level. Only a difference in EMG root mean square slope was found, with a larger increase in the TD group, which was not seen in the CP group.[21] This might indicate that adolescents with CP have problems with the recruitment of motor units on a low force level.[22]

The inconclusive results in previous studies and the small sample size in these studies show the need to further investigate muscle fatigue in the upper limb in adolescents with CP. The aim of this study was therefore to examine the difference in isometric hand grip muscle fatigue between adolescents with unilateral CP aged between 11 and 19 years and age and sex matched TD adolescents and between the dominant and non-dominant hand within both groups. A second aim was to investigate the correlations between maximal strength and muscle fatigue and anthropometric variables in both groups.

MATERIAL AND METHODS

Participants

Adolescents with CP were recruited in the Rehabilitation centre Adelante, in Valkenburg aan de Geul, The Netherlands. Inclusion criteria were 1) a diagnosis of unilateral CP; 2) aged between 11 and 19; 3) Manual Ability Classification Scale between 1 and 3[23] and 4) Zancolli 1, 2a or 2b.[24] The TD adolescents were matched for age and gender and were recruited in the Don Bosco-college Hechtel-Eksel, Belgium. Adolescents with known chronic neurological or musculoskeletal disorders were excluded.

For the CP group the study was approved by the ethics committee of Adelante, the Netherlands. For the TD group the study was approved by the ethics committees of Hasselt and Leuven University. All adolescents and one of the parents gave their informed consent.

Protocol

The adolescents with CP were tested by one physiotherapist and the TD adolescents were tested by one master student physical therapy.

The maximal grip strength test and a 30 seconds isometric endurance task were performed with a digital Jamar dynamometer (E-link, Biometrics Ltd, Newport, UK). Two grips were analysed: hand grip and pinch grip. (Fig.1)

The test person was seated with his/her back against a chair, feet on the ground, elbow in 90° flexion with the forearm fixated by the therapist on the armrest of the chair. Both the forearm and the wrist were positioned in neutral. First the maximal hand grip strength was measured with the grip position of the device adjusted to the size of the hand. During the pinch grip the thumb of the participant was placed on the sensor side of the device and the fingers on the back. In the TD group the hand to be tested first was chosen at random. In the CP group the non-affected hand was tested first.

The participant always performed one practice attempt for familiarization followed by three trials for each hand. The patient was asked to perform a maximal contraction which was held for three seconds maximum.

The endurance task was a 30 seconds maximal isometric contraction. During the test, the participant received visual feedback on the elapsed time, but not on the force. The assessor motivated the participant with repeated encouragements.

Besides the hand tasks also full-body weight and full-body length were measured. The length of the hand from the carpal to the distal point of the longest finger was only measured in the TD group.

Figure 1: Left picture shows the pinch grip, the right picture shows the testing position of the hand grip without fixation of the arm.

Main outcome measurements

1) The maximal strength:

The maximal strength of the hand grip and pinch grip was calculated as the average of the three measurements.

2) Static fatigue index:

The muscle fatigue occurring during both grip tests was analysed with the static fatigue index, as described by Schwid et al. [11]and Surakka et al. [12] in patients with multiple sclerosis.[11,12] The observed force-time curve was compared to the theoretical curve, which would have been observed if there were no fatigue. First the maximal grip force of the observed curve was determined and the time at which this maximal force was produced (Tmax). Subsequently the theoretical curve was created in which the maximal force was constant for 30 seconds. The area under this curve was defined as the hypothetical area under the curve (HAUC), which is represented by the total rectangle in figure 2. Then the actual area under de strength curve (AUC) was analysed as the area under the strength-time curve from Tmax till 30 seconds of the observed force-time curve (Fig 2). Thereafter the static fatigue index (SFI) was calculated with the following formula: 100%*(1-(AUC/HAUC)).

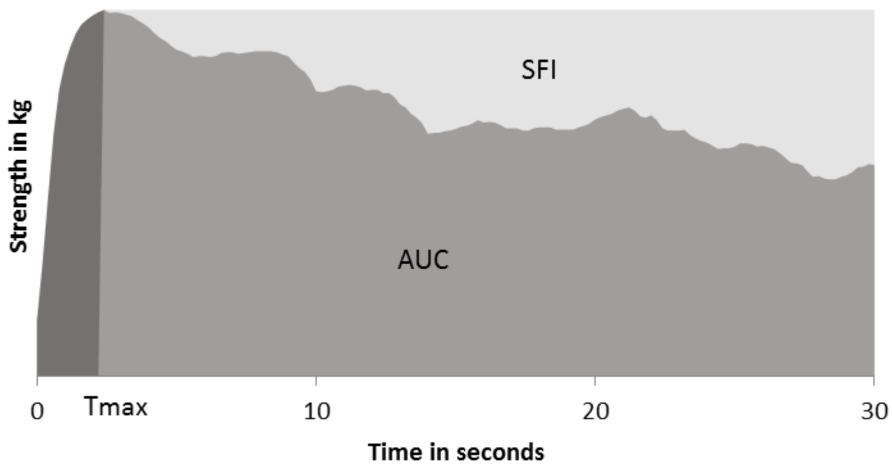

Figure 2: Static fatigue index: (SFI; light grey area) and actual area under the strength curve (AUC; dark gray area).

Statistical analysis

The SFI had a normal distribution in both groups, and therefore parametric statistics were used. Statistical comparison of the SFI between the hands within the groups was done using the paired t-test. An unpaired t-test was used to compare the SFI between the two groups. The results of maximal strength were not normally distributed and therefore non-parametric statistics were applied. The comparison of maximal strength within the groups (between dominant and non-dominant hand) was done using the Wilcoxon signed rank test. For analysing the maximum strength between the two groups a Mann-Whitney U test was used. Furthermore, the Kruskal-Wallis test was applied for comparing the SFI and maximum strength between the different MACS levels. The Spearman correlation coefficient was calculated to determine the correlation between the SFI and maximum strength and between these parameters and age, weight, length and hand length. All statistics were performed using SASJMP PRO 11 software. Significance was accepted at $p \leq 0.05$.

RESULTS

Participants

The participants characteristics of both groups are listed in table I. There were no significant differences between groups weight and total body length. There was a significant difference for hand dominance between both groups (*p*=0.01).

Table I: Subjects characteristics

	CP (n=23)	TD (n=23)
Age, mean, years (SD)	14 (1.43)	14 (1.43)
Age range	11-17	11-17
Gender, female/male, n	12/11	12/11
Hand dominance, left/right, n	12/11	3/20
MACS, 1/2/3, n	7/10/6	\
Weight, mean, kg (SD)	48.81 (9.38)*	51.7 (9.84)
Length, mean, cm (SD)	157.43 (9.62)*	162.3 (11.17)
Length hand, mean, cm (SD)	\	17.7 (1.29)

N: number; SD: standard deviation; * n=21.

Maximal strength

Table II displays the results of maximum strength and SFI of both groups. Figure 3 provides the results regarding maximal strength. For the maximal hand grip strength, the affected hand of the CP group was significantly weaker than the non-affected hand (*p*<0.0001). There was no significant difference in hand grip strength between both hands of the TD group (*p* =0.09). Comparison between the participant groups showed a significantly lower strength for the non-affected hand of the CP group compared with the dominant hand of the TD group (*p*=0.004). This significant difference was also seen between the affected hand of the CP group and the non-dominant hand of the TD group (*p*<0.0001).

The maximal pinch grip strength of the affected hand of the CP group was significantly lower than the strength of the non-affected hand (*p*<0.0001). In the TD-group there was no significant difference between both hands for the maximal pinch grip strength (*p*=0.4). The maximal strength of the pinch grip was significantly lower for the affected hand of the CP group compared with the non-dominant hand of the TD group (*p* <0.0001). There was no significant difference found between the non-affected hand of the CP group and the dominant hand of the TD group for maximal pinch grip strength (*p*=0.9).

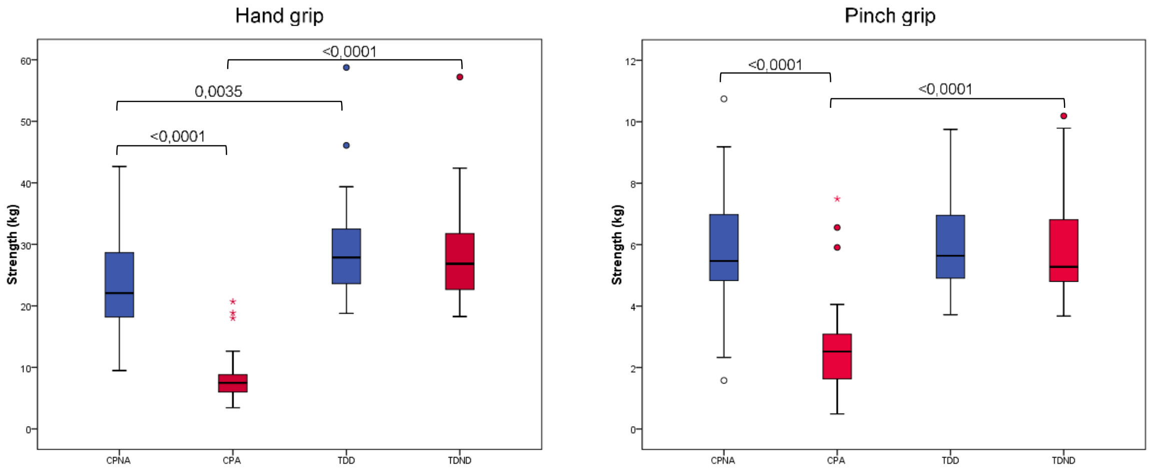

Figure 3: Boxplot of the maximal strength of the hand grip and pinch grip. The boxplot shows: minimum, first quartile, median, third quartile, maximum and outliners. Circles are outliers, very large outliers are marked by an asterisk. The significance *p*-values of the Wilcoxon (signed) rank test are shown. CPNA: cerebral palsy non-affected; CPA: cerebral palsy affected; TDD: typically developing dominant; TDND: typically developing non-dominant.

Static fatigue index

During the pinch grip test the SFI was significantly higher for the affected hand of the CP group, with 57% (SD: 17) compared with 50% (SD: 12) for the non-affected hand (p= 0.016). This difference was not seen during the hand grip test (p=0.3), (mean: CPA 52%; CPNA 54%). No significant difference was found for the SFI between both hands of the TD group for both the hand and pinch grip test. In the TD group the SFI for the dominant and non-dominant hand was respectively 32% (SD: 11), 35% (SD: 8) for the hand grip and 32% (SD: 7) and 34% (SD: 7) for the pinch grip. The SFI was during both grips higher in the CP group compared with the TD group (p<0.0001 for each comparison).

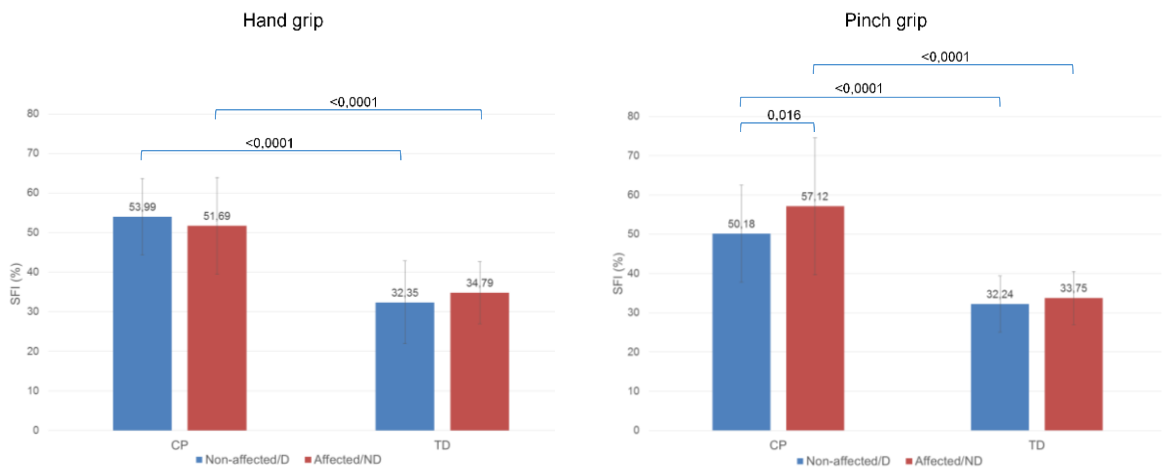

Figure 4: Mean values and standard deviation of the static fatigue index of the hand grip and pinch grip. The *p*-values of the (paired) t-test of significance difference are shown. CP: cerebral palsy; D: dominant; ND: non-dominant; SFI: static fatigue index.

Table II: Maximum strength and SFI for both dominant and non-dominant hand in adolescents with CP and TD adolescents

Maximum strength (median (IQR))						
Grip	CPA	CPNA	*p*-value[a]	TDND	TDD	*p*-value[a]
Hand	7.5 (5.5-8.9)	22.1 (18.1-28.7)	<0.0001[§]	26.8 (22.5-32.5)	27.9 (23.1-33.3)	0.09
Pinch	2.5 (1.6-3.1)	5.5 (4.7-7.0)	<0.0001[§]	5.3 (4.8-6.9)	5.6 (4.8-7.0)	0.41
	CPNA	TDD	*p*-value[a]	CPA	TDND	*p*-value[a]
Hand	22.1 (18.1-28.7)	27.9 (23.1-33.3)	0.004**	7.5 (5.5-8.9)	26.8 (22.5-32.5)	<0.0001[§]
Pinch	5.5 (4.7-7.0)	5.6 (4.8-7.0)	0.88	2.5 (1.6-3.1)	5.3 (4.8-6.9)	<0.0001[§]
Static fatigue index (mean (SD))						
Grip	CPA	CPNA	*p*-value[b]	TDND	TDD	*p*-value[b]
Hand	51.7 (12.2)	54.0 (9.6)	0.33	34.8 (7.8)	32.4 (10.5)	0.06
Pinch	57.1 (17.4)	50.2 (12.3)	0.02*	33.8 (6.8)	32.2 (7.1)	0.19
	CPNA	TDD	*p*-value[b]	CPA	TDND	*p*-value[b]
Hand	54.0 (9.6)	32.4 (10.5)	<0.0001[§]	51.7 (12.2)	34.8 (7.8)	<0.0001[§]
Pinch	50.2 (12.3)	32.2 (7.1)	<0.0001[§]	57.1 (17.4)	33.8 (6.8)	<0.0001[§]

CPA: cerebral palsy affected hand; CPNA: cerebral palsy non-affected hand; IQR: interquartile range; SD: standard deviation; SFI: static fatigue index; TDD: typically developing dominant hand; TDND: typically developing non-dominant hand; [a] p-value of (signed) Wilcoxon; [b] *p*-value of (paired) t-test; *significant with $p \leq 0.05$; **significant with $p < 0.01$; [§]significant with $p < 0.001$.

Correlations

Table III displays the results of the Spearman correlation coefficients that were calculated between age, weight, length, hand length and 1) maximal strength or 2) SFI. Correlations are interpreted as followed: 0.00 to 0.25 little or no relationship, 0.25 to 0.50 fair relationship, 0.50 to 0.75 moderate to good relationship and above 0.75 good to excellent relationship.[25]

1) Typically developing adolescents

In the TD adolescents, the only significant correlation between grip strength and SFI was found for the hand grip of the dominant hand (r=-0.47), meaning that higher maximum strength was associated with lower SFI.

In the TD group significant correlations between maximum strength and anthropometric variables varied between moderate and excellent (r=0.51 - 0.86). Significant correlations between age and hand grip strength were found for the non-dominant (r =0.57) and the dominant hand (r=0.60). Good significant correlations were found between weight and maximum strength of both grips and both hands (r=0.58 - 0.76). Moderate significant correlations were also found between length and maximum strength of both grips and both hands (r=0.54 - 0.73). Significant moderate correlations were found between hand length and maximum strength of both hands for the pinch grip. Excellent significant correlations were seen between hand length and maximum strength of the non-dominant hand grip (r=0.86) and the dominant hand grip (r=0.83).

Furthermore, in the TD group significant negative correlations ranging from fair to moderate were found between SFI and anthropometric variables, meaning that higher SFI was associated with lower anthropometric values (r= -0.44 - -0.61). More specifically, significant correlations were found between age and SFI for the dominant hand grip (r=-0.53), the non-dominant pinch grip (r=-0.46) and the dominant pinch grip (r=-0.61). Significant correlations varying from fair to moderate were found between weight and SFI for the dominant hand grip (r= -0.44) and dominant pinch grip (r=-0.50). No significant correlations were found between length and SFI. Other significant correlations were also found between hand length and SFI of the dominant hand grip (r=-0.48) and the non-dominant pinch grip (r=-0.52).

2) Adolescents with cerebral palsy

No significant correlation was seen between the SFI and maximum strength in the CP group. In this group the correlations with anthropometric variables were lower and only four significant correlations were found, varying between fair and moderate (range r=0.44 - 0.54).
Significant correlations were found between weight and maximal strength of the non-affected hand grip (r=0.48) and pinch grip (r=0.54). Significant correlations were also found between length and maximal strength for the pinch grip of the affected (r=0.54) and non-affected hand (r=0.44).

Table III: Spearman correlation between maximum strength/SFI and age/weight/length/hand length						
			CP-group (n=23)			
	Grip	Hand	Age	Weight[a]	Length[a]	Hand length
Maximum strength	Hand	A	-0.03	0.24	0.35	
		A	0.30	0.48*	0.22	
	Pinch	A	0.23	0.27	0.54*	
		A	0.36	0.54*	0.44*	
			TD-group (n=23)			
	Hand	ND	0.57**	0.71[§]	0.73[§]	0.86[§]
		D	0.60**	0.76[§]	0.67[§]	0.83[§]
	Pinch	ND	0.40	0.65[§]	0.54**	0.51*
		D	0.37	0.58**	0.63**	0.63**
			CP-group (n=23)			
	Grip	Hand	Age	Weight[a]	Length[a]	Hand length
SFI	Hand	A	0.33	0.42	0.19	
		NA	0.34	0.30	0.24	
	Pinch	A	-0.04	0.14	-0.18	
		NA	0.008	0.16	0.05	
			TD-group (n=23)			
	Hand	ND	-0.30	-0.25	-0.26	-0.33
		D	-0.53**	-0.44*	-0.41	-0.48*
	Pinch	ND	-0.46*	-0.37	-0.36	-0.52*
		D	-0.61**	-0.50*	-0.35	-0.30

A: affected; CP: cerebral palsy; D: dominant; NA: non-affected; ND: non-dominant; SFI: static fatigue index; TD: typically developing; * significant with $p \leq 0.05$; ** significant with $p<0.01$; [§] significant with $p<0.001$; [a] n of CP group is 21.

SFI and maximum strength according to MACS

Table IV shows the difference in maximum strength and SFI between the three MACS levels. Kruskal-Wallis test calculated showed no significant difference for the SFI or maximal strength between the three different MACS levels (Table IV).

Table IV: Correlation between MACS and maximum strength/ static fatigue index						
			MACS 1 (n=7)	MACS 2 (n=10)	MACS 3 (n=6)	
	Grip	Hand	Median (IQR)	Median (IQR)	Median (IQR)	*p-value*
Maximum strength	Hand	CPA	8.9 (6.5-18.9)	7.2 (5.4-9.6)	6.8 (3.6-7.6)	0.11
		CPNA	23.9 (20.6-28.7)	18.9 (15.0-23.9)	25.7 (16.7-29.4)	0.24
	Pinch	CPA	2.9 (2.1-5.9)	2.3 (1.2-3.7)	2.2 (1.4-.3.1)	0.41
		CPNA	5.7 (5.1-7.2)	5.0 (4.0-7.1)	6.7 (4.4-7.4)	0.35
SFI	Hand	CPA	45.7 (38.5-59.0)	54.1 (43.3-68.7)	48.8 (44.2-56.2)	0.53
		CPNA	57.5 (44.2-59.5)	54.9 (46.7-61.3)	52.0 (45.6-61.7)	0.88
	Pinch	CPA	47.0 (41.8-68.8)	66.3 (52.5-74.8)	61.0 (46.3-65.7)	0.43
		CPNA	47.4 (41.3-57.1)	50.5 (42.3-65.4)	45.8 (37.7-62.6)	0.77

CPA: cerebral palsy affected; CPNA: cerebral palsy non-affected; IQR: inter quartile range MACS: Manual Ability Classification Scale; *p*-value of Kruskal-Wallis test.

DISCUSSION

This study compared muscle strength and muscle fatigue of the hand and pinch grip between and within a group of 23 adolescents with unilateral CP and 23 age and sex matched TD adolescents. Secondly, the relation between muscle strength and muscle fatigue was investigated as well as the relation with age, weight, body length and hand length. At last, the effect of hand disability level (MACS) on maximal strength and muscle fatigue was investigated in the CP group.

In adolescents with unilateral CP the maximal strength of the affected hand was significantly lower than the strength of the non-affected hand. For both grips the strength of the affected hand was lower than the strength of the non-dominant hand of the TD group. The hand grip strength of the non-affected hand of the CP group was also significantly lower than the strength of the dominant hand of the TD group. This difference in strength between the non-affected hand of the CP group and the dominant hand of the TD group was not found for the pinch grip. These results about maximal strength of the hand and pinch grip is in accordance to several other studies.[20,26,27] Duque et al. [27] found the same results for maximal hand grip and pinch grip strength between children with unilateral CP and TD children aged between 8 and 19 year.[27] Van Meeteren et al.[20] investigated muscle hand grip strength in young adults with CP (mean age 20.6y). They found, in line with our results, a difference in hand grip strength between the affected hand of the adolescents with unilateral CP and the non-dominant hand of the TD adolescents.[20]
Tomhave et al. [26] compared hand and pinch grip strength between children with CP (4-15y) and existing normative data (Ferreira)[28] for age-matched children. They also found a lower strength in the affected hand compared with 1) the non-affected hand and 2) normative data for children for the pinch and hand grip. But in contrast with our study and previous studies[27,20] they did not find a difference in hand grip strength between the non-affected hand and the normative values of TD children. For the pinch grip they found no difference in strength between the non-affected hand of CP group and the normative values with exception for the group from 8 till 10 years. A possible explanation for this difference in results is the age difference between the participants.[17]
It is remarkable that for the hand grip there is a difference in maximal strength between the non-affected hand of the CP adolescents and the dominant hand of the TD adolescents, but that this difference not was found for the pinch grip. Possible explanations for the difference in muscle strength between the affected and non-affected hand in the CP group are already reported, for example differences in muscle volume, cross-sectional area and belly length.[29]

In this study we also investigated muscle fatigue during a 30 seconds isometric hand grip and pinch grip. The SFI was significantly higher for the CP group compared with the TD group, for both grips and for both hands, also the non-affected. Based on the SFI we can conclude that the CP group showed more muscle fatigue than the TD group during a 30 seconds isometric grip task of the hand. Muscle fatigue can occur in both hands due to cardio-respiratory factors.[14] Leunkeu and Ahmaidi [14] found that during a isometric knee-extension of 50% of the maximal strength adolescents with CP (mean age 13y) have a higher oxygen cost compared with the control group (mean age 14y). This higher oxygen cost could be the result of greater motor unit recruiting.[14] Ventilation and heart rate at exhaustion were

also lower in the CP group.[14]
Within both groups there was no significant difference in SFI between both hands, with exception of a higher SFI for the pinch grip of the affected hand in the CP group compared with the non-affected hand. Muscle fatigue during a isometric pinching task has a relation with the oxygenation in the motor cortex. The decrease in oxygenation of the ipsilateral motor cortex occurs because of real-time interaction between the bilateral hemispheres.[30] So it is possible that the participating CP adolescents in our tests experienced more fatigue because of problems with the oxygenation of the brain, but as far as we know there are no previous reports on this theme in CP.
The results of the hand grip SFI were comparable with the results of an earlier study of in young adults with CP (mean age 20.6y) and TD young adults (mean age 21.8). Similar results were found in other neurological diseases, for example in persons with multiple sclerosis. Adults with multiple sclerosis showed a higher SFI compared with healthy control persons. There were no differences found between the SFI of the hands of persons with multiple sclerosis.[31] Adults with prior-polio also had a higher SFI compared with healthy control persons.[32]

Although we would expect the non-affected hand in unilateral CP to show the same muscle fatigue as the hand of the typically developing children, this was not the case. In combination with previous reports, stating that children with unilateral CP have problems in handwriting, fine motor skills [33] as well as sensory deficits [34] of the non-affected hand, these findings indicate that central factors could possibly play a role in the occurrence of fatigue in both hands. Furthermore these results suggest that the 'non-affected' hand should rather be referred to as the 'least-affected' hand.
In literature a lot of explanations are described for problems in the non-affected brain side in unilateral CP which might influence the function of the non-affected hand. A first explanation for impairments at the non-affected side is the 'crowding hypothesis'. Lidzba et al. [33] investigated the crowding hypothesis in children with right-sided spastic CP. They found that patients with right-hemispheric language and left brain injury have problems with visuospatial tasks.[33] The language area is mainly situated in the left brain hemispheric in 85% of the children and 94% of the adults.[34] So it could be possible that in left-hemisphere-damaged children the function of the language area is taken over by the right hemisphere and thereby affecting the other functions of the right hemisphere, such as visuospatial performance. Based on this we could conclude that a one-sided brain injury also affects the working of the non-affected brain side in children with CP and that this could be the cause for a reduced performance of the non-affected side.
A second explanation is the fact that people diagnosed with unilateral CP often have bilateral brain damage.[35,36] Tsao et al. [36] found bilateral brain damage in 42.5% in children diagnosed with congenital spastic hemisphere caused by lesions of the periventricular white matter.[36] Feys et al. [35] found bilateral lesions in 22 of the 53 children with unilateral CP.[35] Based on these studies we could speculate that some of the children in our study also had bilateral brain damage affecting the performance of the non-affected hand but since we had no brain images available we cannot confirm this hypothesis.
A third explanation for the diminishing working of the non-affected side is the fact that also the ipsilateral hemisphere is activated during a unilateral finger task in healthy people. The activation of

the ipsilateral hemisphere is higher when the contraction is higher. [37] If we apply these findings to CP we could hypothesize that the non-affected hand is also controlled by the affected hemisphere. This means that for the treatment of persons with unilateral CP it is important to acknowledge that both hands are affected by the disorder and that treatment should involve both hands. Furthermore, the exact cause of the muscle fatigue in CP should be determined for optimising the treatment. Therefore, further investigation into the pathophysiology in persons with unilateral CP is needed with the focus on the non-affected hand.

In this experiment we also investigated the relation between muscle strength and muscle fatigue. No correlation between maximum strength and SFI was found, neither in the CP group nor in the TD group, with exception of a fair correlation of the dominant hand grip in the TD group (r=-0.47). This result is comparable to the result found by Meldrum et al. [32] They also did not find a correlation between maximum strength and SFI in healthy adults.[32]

Further, the relations of the maximal strength and SFI with age and anthropometric variables (weight, length and hand length) were investigated. In the CP group significant correlations were found between the maximum strength of the non-affected hand for both grips and weight and between the maximum pinch grip strength and length. In the TD group significant positive correlations between maximum strength and anthropometric variables were found and also between hand grip strength and age. The correlations in the TD group between hand grip strength and anthropometric variables were in accordance of several other studies.[38] [39,40] In the CP group there was no correlation found between anthropometric variables and SFI. This is in contrast with the TD group where SFI correlations between fair and moderate were found. Based on the correlations between SFI and age we can conclude that fatigue in CP adolescents does not change from 11 up to 19 years . This is in contrast with TD adolescents where a negative correlation was found, meaning that higher age was associated with a lower SFI and thus less fatigue.

Lastly, the effect of hand disability level (MACS) on maximal strength and muscle fatigue was investigated in the CP group. Contrary to our expectations we found no relation between MACS level and 1) SFI and 2) maximum strength. We did see however a non-significant trend for a lower maximum hand and pinch grip strength of the affected hand for a higher MACS level. This needs to be further investigated in a larger group. A far as we know there are no others studies that investigated the relation between MACS and 1) hand grip strength and 2) SFI during a 30s isometric hand task.

Some limitations in this study need to be addressed. A first limitation is the small sample sizes (n=24). Furthermore, the reliability of muscle fatigue can be questioned. A previous study of van Meeteren et al. [20] analysed the static fatigue index during a 20 seconds isometric hand grip task, and the reliability is moderate (0.59) in healthy young adults.[20] As far as we know there is no information about the reliability of the static fatigue index for adolescents with CP during any task. Neither could we find any published study nor information about the reliability of measurement of the pinch grip strength. Furthermore the pinch grip test was difficult for standardisation, especially when performed by the CP adolescents.

Another limitation is that the results about muscle fatigue cannot be projected to daily activities, because for most hand tasks in daily living a strength of only 20 lb (9 kg) for the hand grip and 5 (2 kg) to 7 lb (3 kg) for the pinch grip is needed[41] and our study measured muscle fatigue during a maximal strength test. Further, the fact that we had no information of the activities in daily living of our study groups should be addressed in subsequent studies.

This study was one of the first studies that investigated muscle fatigue in the upper limb in adolescents with CP. We can conclude that adolescents with unilateral CP experienced more fatigue during a 30s isometric grip task compared with TD adolescents. The findings that also the non-affected hand is involved suggests that more research is needed to understand the pathophysiology contributing to muscle fatigue in adolescents with CP. Based on this study we can also conclude that it is important to include the non-affected hand in physical therapy.

REFERENCES

1 Bax M, Goldstein M, Rosenbaum P, Leviton A, Paneth N, Dan B, Jacobsson B, Damiano D, Executive Committee for the Definition of Cerebral P. Proposed definition and classification of cerebral palsy, April 2005. *Developmental medicine and child neurology* 2005; **47**: 571-6.

2 Surveillance of Cerebral Palsy in E. Surveillance of cerebral palsy in Europe: a collaboration of cerebral palsy surveys and registers. Surveillance of Cerebral Palsy in Europe (SCPE). *Developmental medicine and child neurology* 2000; **42**: 816-24.

3 Jahnsen R, Villien L, Stanghelle JK, Holm I. Fatigue in adults with cerebral palsy in Norway compared with the general population. *Developmental medicine and child neurology* 2003; **45**: 296-303.

4 Bruno AE, Sethares KA. Fatigue in Parkinson disease: an integrative review. *J Neurosci Nurs* 2015; **47**: 146-53.

5 Wessely S. The epidemiology of chronic fatigue syndrome. *Epidemiologic reviews* 1995; **17**: 139-51.

6 Kluger BM, Krupp LB, Enoka RM. Fatigue and fatigability in neurologic illnesses: proposal for a unified taxonomy. *Neurology* 2013; **80**: 409-16.

7 Bigland-Ritchie B, Johansson R, Lippold OC, Smith S, Woods JJ. Changes in motoneurone firing rates during sustained maximal voluntary contractions. *The Journal of physiology* 1983; **340**: 335-46.

8 Gandevia SC. Spinal and supraspinal factors in human muscle fatigue. *Physiological reviews* 2001; **81**: 1725-89.

9 Leunkeu AN, Keefer DJ, Imed M, Ahmaidi S. Electromyographic (EMG) analysis of quadriceps muscle fatigue in children with cerebral palsy during a sustained isometric contraction. *Journal of child neurology* 2010; **25**: 287-93.

10 O'Sullivan S. *Physical Rehabilitation.* Philadelphia: F.A. Davis Company; 2007.

11 Schwid SR, Thornton CA, Pandya S, Manzur KL, Sanjak M, Petrie MD, McDermott MP, Goodman AD. Quantitative assessment of motor fatigue and strength in MS. *Neurology* 1999; **53**: 743-50.

12 Surakka J, Romberg A, Ruutiainen J, Virtanen A, Aunola S, Maentaka K. Assessment of muscle strength and motor fatigue with a knee dynamometer in subjects with multiple sclerosis: a new fatigue index. *Clinical rehabilitation* 2004; **18**: 652-9.

13 Leunkeu AN, Gayda M, Nigam A, Lecoutre N, Ahmaidi S. Cardiopulmonary exercise data during quadriceps isometric contraction sustained to fatigue in children with cerebral palsy. *Isokinetics and Exercise Science* 2009; **17**: 27-33.

14 Leunkeu AN, Ahmaidi S. Longitudinal assessment of muscle function and oxygen cost during isometric testing in children with cerebral palsy. *Isokinetics and Exercise Science* 2012; **20**: 107-13.

15 Eken MM, Dallmeijer AJ, Houdijk H, Doorenbosch CA. Muscle fatigue during repetitive voluntary contractions: a comparison between children with cerebral palsy, typically developing children and young healthy adults. *Gait & posture* 2013; **38**: 962-7.

16 Moreau NG, Li L, Geaghan JP, Damiano DL. Fatigue Resistance During a Voluntary Performance Task Is Associated With Lower Levels of Mobility in Cerebral Palsy. *Archives of physical medicine and rehabilitation* 2008; **89**: 2011-6.

17 Larsson B, Karlsson JS, Gerdle B. Muscle performance during maximum repeated knee extensions in children with hemiplegic cerebral palsy. *Isokinetics and Exercise Science* 2008; **16**: 221-30.

18 Lemmens RJ, Janssen-Potten YJ, Timmermans AA, Defesche A, Smeets RJ, Seelen HA. Arm hand skilled performance in cerebral palsy: activity preferences and their movement components. *BMC neurology* 2014; **14**: 52.

19 Arnould C, Penta M, Thonnard JL. Hand impairments and their relationship with manual ability in children with cerebral palsy. *Journal of rehabilitation medicine* 2007; **39**: 708-14.

20 van Meeteren J, van Rijn RM, Selles RW, Roebroeck ME, Stam HJ. Grip strength parameters and functional activities in young adults with unilateral cerebral palsy compared with healthy subjects. *J Rehabil Med* 2007; **39**: 598-604.

21 Doix AC, Gulliksen A, Braendvik SM, Roeleveld K. Fatigue and muscle activation during submaximal elbow flexion in children with cerebral palsy. *Journal of electromyography and kinesiology : official journal of the International Society of Electrophysiological Kinesiology* 2013; **23**: 721-6.

22 Rose J, McGill KC. Neuromuscular activation and motor-unit firing characteristics in cerebral palsy. *Developmental medicine and child neurology* 2005; **47**: 329-36.

23 Eliasson AC, Krumlinde-Sundholm L, Rosblad B, Beckung E, Arner M, Ohrvall AM, Rosenbaum P. The Manual Ability Classification System (MACS) for children with cerebral palsy: scale development and evidence of validity and reliability. *Developmental medicine and child neurology* 2006; **48**: 549-54.
24 Zancolli EA, Goldner LJ, Swanson AB. Surgery of the spastic hand in cerebral palsy: report of the Committee on Spastic Hand Evaluation (International Federation of Societies for Surgery of the Hand). *The Journal of hand surgery* 1983; **8**: 766-72.
25 Portney W. *Foundations of Clinical Research: Applications to Practice.* New Jersey: Julie Levin Alexander; 2013.
26 Tomhave WA, Van Heest AE, Bagley A, James MA. Affected and contralateral hand strength and dexterity measures in children with hemiplegic cerebral palsy. *The Journal of hand surgery* 2015; **40**: 900-7.
27 Duque J, Thonnard JL, Vandermeeren Y, Sebire G, Cosnard G, Olivier E. Correlation between impaired dexterity and corticospinal tract dysgenesis in congenital hemiplegia. *Brain* 2003; **126**: 732-47.
28 Ferreira ACC SA, Mazzer N, Barbieri CH, Elui VMC, Fonseca MCR. Grip and pinch strength in healthy children and adolescents. Acta Ortop Bras.; 2011. 92-7.
29 Barrett RS, Lichtwark GA. Gross muscle morphology and structure in spastic cerebral palsy: a systematic review. *Developmental medicine and child neurology* 2010; **52**: 794-804.
30 Shibuya K, Kuboyama N. Human motor cortex oxygenation during exhaustive pinching task. *Brain Res* 2007; **1156**: 120-4.
31 Severijns D, Lamers I, Kerkhofs L, Feys P. Hand grip fatigability in persons with multiple sclerosis according to hand dominance and disease progression. *Journal of rehabilitation medicine* 2015; **47**: 154-60.
32 Meldrum D, Cahalane E, Conroy R, Guthrie R, Hardiman O. Quantitative assessment of motor fatigue: normative values and comparison with prior-polio patients. *Amyotroph Lateral Scler* 2007; **8**: 170-6.
33 Lidzba K, Staudt M, Wilke M, Krageloh-Mann I. Visuospatial deficits in patients with early left-hemispheric lesions and functional reorganization of language: consequence of lesion or reorganization? *Neuropsychologia* 2006; **44**: 1088-94.
34 Wood AG, Harvey AS, Wellard RM, Abbott DF, Anderson V, Kean M, Saling MM, Jackson GD. Language cortex activation in normal children. *Neurology* 2004; **63**: 1035-44.
35 Feys H, Eyssen M, Jaspers E, Klingels K, Desloovere K, Molenaers G, De Cock P. Relation between neuroradiological findings and upper limb function in hemiplegic cerebral palsy. *Eur J Paediatr Neurol* 2010; **14**: 169-77.
36 Tsao H, Pannek K, Fiori S, Boyd RN, Rose S. Reduced integrity of sensorimotor projections traversing the posterior limb of the internal capsule in children with congenital hemiparesis. *Res Dev Disabil* 2014; **35**: 250-60.
37 Shibuya K, Kuboyama N, Tanaka J. Changes in ipsilateral motor cortex activity during a unilateral isometric finger task are dependent on the muscle contraction force. *Physiol Meas* 2014; **35**: 417-28.
38 Ploegmakers JJ, Hepping AM, Geertzen JH, Bulstra SK, Stevens M. Grip strength is strongly associated with height, weight and gender in childhood: a cross sectional study of 2241 children and adolescents providing reference values. *J Physiother* 2013; **59**: 255-61.
39 Jurimae T, Hurbo T, Jurimae J. Relationship of handgrip strength with anthropometric and body composition variables in prepubertal children. *Homo* 2009; **60**: 225-38.
40 Hager-Ross C, Rosblad B. Norms for grip strength in children aged 4-16 years. *Acta Paediatr* 2002; **91**: 617-25.
41 Philips CA. Rehabilitation of the patient with rheumatoid hand involvement. *Physical therapy* 1989; **69**: 1091-8.

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