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Alterations of treatment-naïve pelvis and thigh muscle morphology in children with cerebral palsy

Abir Massaad ^a, Ayman Assi ^{a,b,*}, Ziad Bakouny ^a, Aren Joe Bizdikian ^a, Wafa Skalli ^b, Ismat Ghanem ^a

ABSTRACT

Lower limb (LL) muscle morphology and growth are altered in children with cerebral palsy (CP). Muscle alterations differ with age and with severity of motor impairment, classified according to the gross motor classification system (GMFCS). Muscle alterations differ also with orthopedic intervention, frequently performed at the level of the shank muscles since an early age, such as the gastrocnemius. The aim was to investigate the alterations of treatment-naïve pelvis and thigh muscle lengths and volumes in children with GMFCS levels I and II, of varying ages.

17 children with CP (GMFCS I: N = 9, II: N = 8, age: 11.7 ± 4 years), age-matched to 17 typically developing (TD) children, underwent MRI of the LL. Three-dimensional reconstructions of the muscles were performed bilaterally. Muscle volumes and lengths were calculated in 3D and compared between groups. Linear regression between muscle volumes and age were computed.

Adductor-brevis and gracilis lengths, as well as rectus-femoris volume, were decreased in GMFCS I compared to TD (p < 0.05). Almost all the reconstructed muscle volumes and lengths were found to be altered in GMFCS II compared to TD and GMFCS I. All muscle volumes showed significant increase with age in TD and GMFCS I (\mathbb{R}^2 range: 0.3–0.9, p < 0.05). Rectus-femoris, hamstrings and adductor-longus showed reduced increase in the muscle volume with age in GMFCS II when compared to TD and GMFCS I.

Alterations of treatment-naïve pelvis and thigh muscle volumes and lengths, as well as muscle growth, seem to increase with the severity of motor impairment in ambulant children with CP.

Keywords: Cerebral palsy Treatment-naïve Muscle alterations Muscle growth Pelvis Thigh Lower limbs 3D reconstruction MRI

1. Introduction

Cerebral palsy is a common neurological disorder with a prevalence ranging between 1.5 and 2.5 per 1000 births according to the Surveillance of Cerebral Palsy In Europe (SCPE, 2002). Spasticity, contractures (Farmer and James, 2001), lack of muscle selectivity (Fowler et al., 2010), muscle weakness (Elder et al., 2003) and motor disability are usually encountered in these patients (Bax et al., 2005). A large proportion of children with CP are ambulant (SCPE, 2002) and present alterations in their walking abilities that can be classified according to gross motor classification system (GMFCS) levels (Palisano et al., 2008). Walking abilities in children with CP are highly related to the reduction in lower limb (LL) muscle force (Ross and Engsberg, 2007), which is known to be correlated to lower limb muscle morphology (Moreau et al., 2012,

2010). Muscle morphology has been previously shown to be progressively affected during growth in these patients (Barber et al., 2016), in part due to the reduction in physical activity and motion abnormalities (Karagounis and Hawley, 2010).

Only a few studies, which included only children with histories of various medical and surgical interventions, have investigated muscle lengths (Fry et al., 2003; Handsfield et al., 2016; Oberhofer et al., 2010), volumes (Handsfield et al., 2016; Noble et al., 2014; Oberhofer et al., 2010), or cross-sectional areas (Handsfield et al., 2016) of the LL in children with CP, with conflicting results. Moreover, these parameters have never been studied in children with different GMFCS levels. Furthermore, muscle lengths and volumes are known to be affected by orthopedic interventions, which are often performed from a very young age (casting, botulinum toxin, soft tissue surgery) (Handsfield et al., 2016). There are currently no studies evaluating the natural evolution of the muscular pathology in children with CP by eliminating the bias of surgical and medical interventions on pelvis and thigh muscles. Furthermore, while it is known that volume alterations in these children become more significant with age, this was only reported for the

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gastrocnemius medius (Barber et al., 2016, 2011), and possible alterations for the remaining pelvis and thigh muscles have not yet been investigated.

The aim of this study was to investigate the volume and length alterations of treatment-naïve pelvis and thigh muscles in ambulant children with GMFCS levels I and II, of varying ages.

2. Methods

2.1. Participants

This is an IRB approved (CEHDF 504) cross-sectional study of children with CP who underwent an MRI exam of the LL. Children with CP were recruited from our university hospital, where patients consulted for orthopedic care and were invited to participate in this study. Children with no history of orthopedic interventions in the pelvis and thigh (proximal leg) muscles, such as botulinum toxin injections, casting, or surgery, were enrolled. Typically developing (TD) children were enrolled in this study and formed the control group. The parents of all participants approved and signed a written informed consent form. Demographics (age, weight, height) and physical examination data of muscle spasticity (Bohannon and Smith, 1987), range of motion (Viehweger et al., 2007), and manual muscle testing (Kendall et al., 1993) of CP children were collected and reported as numerical data.

2.2. Data acquisition and processing

Height, lower limb lengths in standing position, and mass were measured using a stadiometer, a measuring tape, and a weight scale respectively. MRI data were collected on a 3 Tesla General Electric® system. MRI slices were taken from the pelvis to the tip of the toes while the subjects lay supine on the scanner bed with their ankles, knees, and hips in a neutral and relaxed position. All participants were strapped to the MRI table at the level of the hips, knees, and ankles to stabilize the limb in position during the acquisition.

The echo gradient protocol was used with a flip angle of 70° : TE/TR = 10 ms/220 ms, slice thickness = 1 mm, gap = 4 mm, Nex = 2. The body coil antenna was used for all acquisitions. Two consecutive sequences during the same acquisition were obtained for each subject. The first one for the pelvis and thighs and the second one for the shanks and feet. The scanner bed was moved automatically between the two sequences without modification of the position of the subject. The average time for the acquisition was 30 min.

Muscles were reconstructed in 3D using a specific software (Arts et Métiers ParisTech, Paris, France). Muscle belly contours were detected on the MRI slices between the proximal and the distal muscle-tendon junctions. The muscle-tendon junction was identified as the level where muscle fibers (dark color) were no longer visible and the tendon became visible (light color). The 3D reconstruction was semi-automatic: Muscle contours are delimited on a reduced number of axial slices (30%). Each contour is then approximated to an ellipse characterized by its centroid, width, length, and orientation in the 2D plane of the slice. Afterwards, the evolution of centroids, widths, lengths, and orientations, from the first to the last delimited slices, is modelled using cubic spline interpolation. Missing slices (non-delimited ones) are later created using the interpolated centroids, widths, lengths, and orientations. Finally, the operator verifies each slice and adjusts the muscle's contour if needed.

This technique has been previously described and validated (Assi et al., 2008; Hausselle et al., 2014; Jolivet et al., 2008). The following pelvis and thigh muscles were reconstructed bilaterally:

vastus intermedius, vastus lateralis, vastus medialis, rectus femoris, femoral biceps brevis and longus, semimembranosus, semitendinosus, and adductors brevis, magnus, longus and gracilis. Muscle lengths and volumes were calculated using Matlab[®].

2.3. Statistical analysis

The unaffected side of children with hemiplegia was excluded from the statistical analysis. Demographic characteristics were compared between the groups of TD children and children with CP with GMFCS levels I and II using a Kruskal-Wallis test followed by Conover-Iman pairwaise comparisons with a Bonferroni correction.

In order to compare the muscle morphology (length and volume) of TD and children with CP (GMFCS levels I and II) while controlling for possible confounding factors, a one-way analysis of covariance (ANCOVA) was performed. The comparisons of muscle volumes between the 3 groups were performed while controlling for age and weight * height (considered as covariates) (Handsfield et al., 2014), whereas the comparisons of muscle lengths were computed while controlling for age and lower limb lengths (considered as covariates). The ANCOVA analysis was followed by Dunn-Sidak pairwise comparisons on estimated marginal means that have been adjusted for covariates by the model.

The distributions of muscle volumes and lengths in children with CP were compared to those in TD children. First, muscle volumes were normalized to the height * weight of the subjects and lengths were normalized to LL lengths. For each muscle, the bottom 5th percentile of the lengths and volumes in TD children were calculated. Muscles in children with CP presenting lengths and volumes below the values of the bottom 5th percentile in TD children, were classified as abnormally low. Fisher's test was used to study the differences in distributions between the CP (GMFCS levels I and II) and TD groups into 2 classes (normal and abnormally low) and the effect size was quantified by Cramer's V (CrV) coefficient.

The linear regression between non-normalized muscle volume for each individual muscle and for age was studied for both TD and CP groups. In order to assess whether the relationship between CP muscle volume and age was similar to that between TD muscle volume and age, the muscle volumes of children with CP were plotted on the graph of the TD linear regression. Two groups were then defined according to the 95% confidence interval of the linear regression between volume and age in TD subjects: inside or above (first group), and below (second group) the 95% CI. The differences in distribution into the latter 2 groups in TD and children with CP (I and II) were studied using Fisher's test.

Statistical analysis was performed using SPSS® (IBM, New York, USA) and XIstat® (Addinsoft, Paris, France). The threshold of statistical significance was set at α = 0.05.

3. Results

3.1. Demographics

17 children with CP (28 limbs) and 17 TD children (34 limbs) were enrolled in this study and had their pelvis and thigh muscles reconstructed in 3D (Fig. 1).

The demographics of the two groups are represented in Table 1. The comparisons of age, weight, and height between the TD group and children with CP (GMFCS levels I and II) showed no significant differences (Table 1). The results of the physical examination of muscle spasticity, range of motion, and manual muscular testing

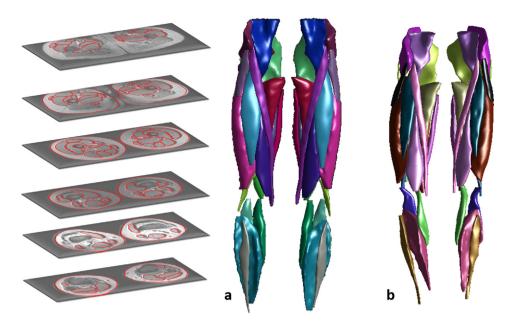


Fig. 1. Three-dimensional (3D) reconstructions of the lower limb muscles in (a) a typically developing (TD) child and (b) a child with cerebral palsy (CP) presenting a spastic diplegia.

Table 1Demographic characteristics of the typically developing children (TD) and children with spastic cerebral palsy (CP). Distribution of the children with spastic CP according to the Gross Motor Function Classification System (GMFCS).

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	TD children	CP children	CP children	TD vs GMFCS I	TD vs GMFCS II	GMFCS I vs GMFCS II
		GMFCS I	GMFCS II	_		
		mean ± SD	mean ± SD	p-value	p-value	p-value
		min-max	min max			
N	17	9	8			
Hemiplegia (N)		5	1			
Diplegia (N)		4	7			
Age	10.8 ± 2.5	11.4 ± 4	11.8 ± 3.8	0.762	0.535	0.804
	8.5-17	6.3-18.7	7.6-19.6			
Weight (kg)	45.7 ± 13.4	41.7 ± 18.2	46.5 ± 18.3	0.352	0.938	0.387
	32-75	15-68	22-70			
Height (cm)	146 ± 13	141.4 ± 17.5	146 ± 13.4	0.535	0.261	0.148
	132-183	113-173	119-160			

of children with CP (GMFCS levels I and II) are represented in Table 2.

3.2. Mean comparisons of muscle volumes and lengths in children with GMFCS levels I and II

The volumes of all the reconstructed muscles were significantly reduced in children with GMFCS level II compared to TD children (all p < 0.05) except for the femoral biceps brevis, adductor magnus, and gracilis. Only the rectus femoris presented a reduced volume in children with GMFCS level I compared to TD (p = 0.047; Table 3). The rectus femoris, femoral biceps longus, semimembranosus, semitendinosus, and adductor longus volumes were significantly reduced in children with GMFCS level II compared to I (all p < 0.05; Table 3).

The lengths of the rectus femoris, semimembranosus, adductors brevis, adductor longus, and gracilis were found to be significantly reduced in children with GMFS level II compared to TD children (p = 0.001). Only the adductor brevis and the gracilis presented a significantly reduced length in children with GMFCS level I compared to TD (p = 0.015, p = 0.002, respectively; Table 3). Only the rectus femoris presented a significantly reduced length in children with GMFCS level II compared to those with GMFCS level I (p = 0.017; Table 3).

3.3. Distribution of muscle volumes and lengths in children with GMFCS levels I and II according to TD children

The volumes of the rectus femoris, hamstrings (femoral biceps longus and semimembranosus), adductor brevis, and adductor longus were significantly more frequently classified as abnormally low in children with GMFCS level II (10/15, 12/15, 8/15, 4/15, 9/15 respectively) compared to TD children (2/34 for all muscles, representing the bottom 5th percentile) and children with GMFCS level I (2/13, 4/13, 2/13, 0/13, 1/13 respectively; all p < 0.05; Fig. 2). The rectus femoris, hamstrings (femoral biceps longus and semimembranosus), and adductor longus volume were found to be significantly more frequently classified as abnormally low in children with GMFCS level I (2/13, 4/13, 2/13, 1/13 respectively) compared to TD (2/34; all p < 0.05). The CrV coefficient ranged between 0.3 and 0.7 (all p < 0.05).

The lengths of the rectus femoris, adductor brevis, adductor longus, and gracilis were significantly more frequently classified as abnormally low in children with GMFCS level II (9/15, 5/15, 8/15, 10/15 respectively) compared to TD children (2/34) and to children with GMFCS level I (1/13, 4/13, 3/13, 3/13 respectively; all p < 0.05; Fig. 3). The CrV coefficient ranged between 0.3 and 0.6 (all p < 0.05).

Table 2
Results of physical examination of children with GMFCS levels I and II: Modified Ashworth scale (MAS) for spasticity testing, Range of motion (ROM), Manual muscle testing (MMT), Knee flexed (KF), knee extended (KE).

MAS (scale from 0 t	o 5)		Passive ROM (degre	es)
GMFCS I (SD)	GMFCS II (SD)		GMFCS I (SD)	GMFCS II (SD)
0.3 (0.5)	1.4 (0.8)	Hip abduction KF	35 (9)	28.7 (14.1)
1.5 (1.4)	2.4 (0.6)	Hip Abduction KE	25.8 (10.4)	20.7 (14.5)
1.2 (1.5)	2 (0.7)	Hip Extension KE	0.9 (7.4)	-2.3(9.9)
0.9 (1.1)	1.9 (0.8)	Hip extension KF	-9 (5.8)	-13.8(15.3)
MMT (scale from 0	to 5)	Hip Internal rotation	35.4 (7.2)	50.7 (11.6)
4.6 (0.5)	3.3 (0.5)	Hip external rotation	35 (14.6)	26.3 (12.2)
4.5 (0.8)	2.8 (0.8)	Unilateral pop. angle	54.6 (26.1)	68.7 (26.9)
4.2 (1.1)	2.8 (0.5)	bilateral pop. angle	36.5 (19.3)	63.8 (29.6)
	MAS (scale from 0 t GMFCS I (SD) 0.3 (0.5) 1.5 (1.4) 1.2 (1.5) 0.9 (1.1) MMT (scale from 0 4.6 (0.5) 4.5 (0.8)	MAS (scale from 0 to 5) GMFCS I (SD) 0.3 (0.5) 1.4 (0.8) 1.5 (1.4) 2.4 (0.6) 1.2 (1.5) 2.9 (0.7) 0.9 (1.1) 1.9 (0.8) MMT (scale from 0 to 5) 4.6 (0.5) 4.5 (0.8) 3.3 (0.5) 4.8 (0.8)	MAS (scale from 0 to 5) GMFCS I (SD) GMFCS II (SD) 0.3 (0.5) 1.4 (0.8) Hip abduction KF 1.5 (1.4) 2.4 (0.6) Hip Abduction KE 1.2 (1.5) 2 (0.7) Hip Extension KE 0.9 (1.1) 1.9 (0.8) Hip extension KF MMT (scale from 0 to 5) Hip Internal rotation 4.6 (0.5) 3.3 (0.5) Hip external rotation 4.5 (0.8) 2.8 (0.8) Unilateral pop. angle	MAS (scale from 0 to 5) Passive ROM (degree GMFCS I (SD) GMFCS I (SD) GMFCS II (SD) 0.3 (0.5) 1.4 (0.8) Hip abduction KF 35 (9) 1.5 (1.4) 2.4 (0.6) Hip Abduction KE 25.8 (10.4) 1.2 (1.5) 2 (0.7) Hip Extension KE 0.9 (7.4) 0.9 (1.1) 1.9 (0.8) Hip extension KF -9 (5.8) MMT (scale from 0 to 5) Hip Internal rotation 35.4 (7.2) 4.6 (0.5) 3.3 (0.5) Hip external rotation 35 (14.6) 4.5 (0.8) 2.8 (0.8) Unilateral pop. angle 54.6 (26.1)

Modified Ashworth Scale (MAS)

0 = no increase in muscle tone.

- 1 = Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension.
- 2 = Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM.
- 3 = More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved.
- 4 = Considerable increase in muscle tone, passive movement difficult.
- 5 = Affected part(s) rigid in flexion or extension.

Manual Muscle Testing (MMT)

0 = no contractions felt in the muscle.

T = Trace.

Movement in horizontal plane

- 1 = Moves through partial range of motion.
- 2 = Moves through complete range of motion.

Antigravity position

- 3 = Moves through partial range of motion.
- 4 = Gradual release from test position.
- 5 = Holds test position (no added pressure).
- 6 = Holds test position against slight pressure.
- 7 = Holds test position against slight to moderate pressure.
- 8 = Holds test position against moderate pressure.
- 9 = Holds test position against moderate to strong pressure.
- 10 = Holds test position against strong pressure.

Table 3Belly muscle volumes and lengths of typically developing children and children with cerebral palsy.

	Adjusted volumes ¹ (cm ³)						Adjusted lengths ² (cm)					
	TD (SD)	GMFCS I (SD)	GMFCS II (SD)	TD vs GMFCS I (p value)	TD vs GMFCS II (p value)	GMFCS I vs II (p value)	TD (SD)	GMFCS I (SD)	GMFCS II (SD)	TD vs GMFCS I (p value)	TD vs GMFCS II (p value)	GMFCS I vs II (p value)
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Vastus	247	227	185	0.960	0.006	0.228	28	27	26	1.000	0.201	0.871
intermedius	(61)	(62)	(62)				(3)	(3)	(3)			
Vastus	312	290	247	0.864	0.005	0.240	27	27	26	1.000	1.000	1.000
lateralis	(64)	(64)	(64)				(3)	(3)	(3)			
Vastus	193	184	160	1.000	0.023	0.303	26	26	26	1.000	1.000	1.000
medialis	(37)	(37)	(37)				(3)	(3)	(3)			
Rectus	132	111	85	0.047	<0.001	0.033	25	25	23	1.000	0.001	0.017
femoris	(26)	(26)	(26)				(2)	(2)	(2)			
Femoral	40	43	34	1.000	0.547	0.224	14	16	16	0.389	0.34	0.230
biceps brevis	(13)	(13)	(13)				(3)	(4)	(3)			
Femoral	79	70	50	0.214	<0.001	0.003	18	19	18	0.329	1.000	1.000
biceps longus	(14)	(15)	(14)				(1)	(1)	(2)			
Semi	98	90	68	0.860	<0.001	0.032	22	21	19	0.880	0.036	0.71
membranosus	(22)	(22)	(22)				(3)	(3)	(3)			
Semi	85	81	61	1.000	<0.001	0.017	23	23	21	1.000	0.114	0.351
tendinosus	(18)	(18)	(18)				(2)	(2)	(2)			
Adductor	52	48	38	0.957	0.004	0.196	10	8	8	0.015	0.006	1.000
brevis		(14)	(13)				(2)	(2)	(2)			
	(13)	()	()				(-)	(-)	(-)			
Adductor	62	56	53	0.478	<0.001	<0.001	13	12	10	0.1	<0.001	0.126
longus		(13)	(13)				(2)	(2)	(2)			
	(13)	()	()				(-)	(-)	(-)			
Adductor	244	240	213	1.000	0.211	0.589	21	22	20	1.000	0.717	0.273
magnus	(53)	(53)	(53)	1.500	0,211	5.505	(3)	(3)	(3)		J., 17	5.275
Gracilis	44	47	38	1.000	0.342	0.122	23	21	20	0.002	<0.001	0.369
GIACIIIS	(11)	(11)	(11)	1.000	0,372	0.122	(2)	(2)	(2)	0.002	100.00	0,000

¹ Adjusted volumes for age and weight * height (covariates).

² Adjusted lengths for age and lower limb lengths (covariates).

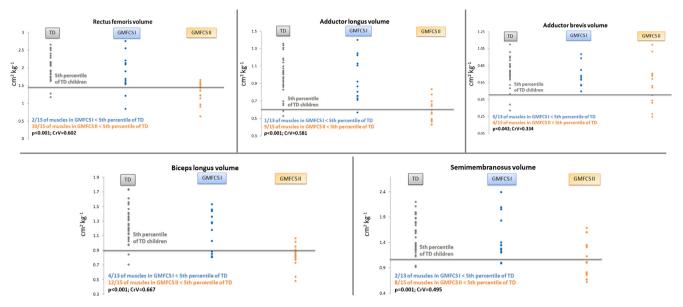


Fig. 2. Distributions of the muscle belly volumes (normalized to weight * height) in children with GMFCS levels I and II with regard to TD children.

3.4. Muscle volume and age in children with CP

Muscle volumes significantly increased with age for all the reconstructed muscles in TD children (R^2 ranged between 0.33 and 0.59, all p < 0.05). As for children with GMFCS level I, all the reconstructed muscle volumes significantly increased with age

 $(R^2 \text{ ranged between 0.35 and 0.89, all p < 0.05)}$. In children with GMFCS level II, all the reconstructed muscle volumes significantly increased with age (R^2 ranged between 0.31 and 0.88, all p < 0.05), except for the semitendinosus and semimembranosus.

When the relationship between muscle volume and age in TD children was plotted, the distribution of volumes in children with

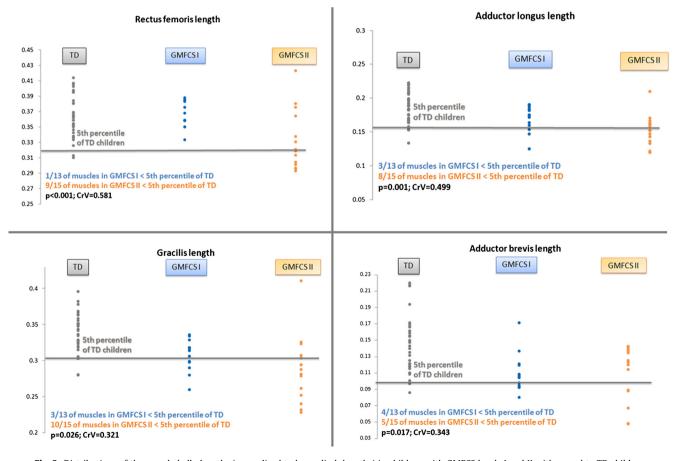


Fig. 3. Distributions of the muscle belly lengths (normalized to lower limb lengths) in children with GMFCS levels I and II with regard to TD children.

Growth of muscle volumes (cm³) with age (years) in TD children with regard to children with CP (GMFCS I & II)

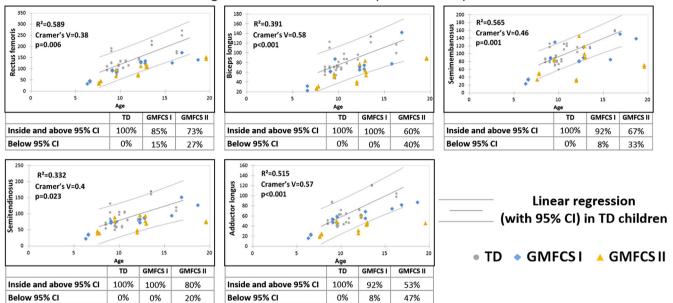


Fig. 4. Linear regression between muscle belly volumes and age in TD children. The muscle volumes of CP children with GMFCS levels I and II were displayed on the graphs.

CP was found to be shifted towards the lower limit of the 95% CI of the linear regression (Fig. 3). Children with GMFCS level II, but not those with GMFCS level I, had the following muscles significantly shifted below the 95% CI: rectus femoris, femoral biceps longus, semimembranosus, semitendinosus, and adductor longus; CrV coefficient ranged between 0.38 and 0.58 (Fig. 4).

4. Discussion

Lower limb muscle morphology and growth are known to be altered in children with cerebral palsy (CP); these alterations could be more pronounced with orthopedic intervention. Treatmentnaïve pelvis and thigh muscle volumes and lengths in children or varying ages with GMFCS levels I and II were investigated in this study, thus representing their natural history. Muscle morphology seemed to be more affected when motor impairment increased in children with CP. While the pelvis and thigh muscles of children with GMFCS level I were found to follow a similar morphological growth pattern to that of TD children, several muscles in children with GMFCS level II were found to have less pronounced morphological growth with age.

Children with GMFCS level I presented similar average muscle lengths at the thigh compared to TD children, except for the adductor brevis and gracilis, which were found to be significantly shorter (Table 3). Although the mean length of the adductor longus did not significantly differ between children with GMFCS level I and TD children, it tended to be shorter without reaching statistical significance (as shown in the distribution analysis in Fig. 3). These results could indicate that among thigh muscles, the adductors (gracilis, adductor brevis and longus) might be the most likely to be shortened in children with GMFCS level I. It is important to mention that the calculated lengths in this study are those of the muscle bellies. It was shown in the literature that children with CP present not only shortened muscle bellies when compared to TD, but also longer tendons (Wren et al., 2010). In sum, the length of the muscle-tendon unit is altered in children with CP. Orthopedic, medical or manual techniques attempting to lengthen the shortened muscles, and thereby increasing the range of motion of the hip and the response to stretch reflex (Bar-On et al., 2014), could help improve walking abilities in this group.

Moreover, mean thigh muscle volumes were similar between TD children and children with GMFCS level I, except for the rectus femoris (Table 3). These results may indicate that the high level of functional ability in children with GMFCS level I could promote a natural evolution of normal growth for the volumes of most thigh muscles. However, the rectus femoris, hamstrings (femoral biceps longus and semimembranosus), and adductor longus and brevis muscles showed significant heterogeneity within the GMFCS level I group, with a significant proportion of children in this group having abnormally low volumes for these muscles (Fig. 2). While all the reconstructed muscles showed a significant increase with age, the rectus femoris, semimembranosus, and the adductor longus were the most likely to present reduced volume during growth (Fig. 4). These results should be taken into account during treatment planning (botox injection, tenotomy...) for these muscles in children with GMFCS level I, treatments that may further reduce their volume, and subsequently weaken them, and therefore affect these children's walking abilities.

Both mean muscle volumes and lengths were found to be significantly decreased in children with GMFCS level II compared to TD children for most of the reconstructed muscles (Table 3). The results obtained in the current study represent the natural evolution of muscle lengths and volumes for hip adductors, and knee extensors and flexors in this group of children with GMFCS level II. In particular, the volume of the rectus femoris, hamstrings (femoral biceps longus, semimembranosus and semimembranosus), and adductor longus was significantly reduced in children with GMFCS level II compared to those with GMFCS level I (Table 3). These findings are in accordance with those of Noble et al., 2014 for the rectus femoris, semitendinosus, and semimembranosus. In children with GMFCS level II, a significantly larger proportion of muscle volumes and lengths were classified as abnormally low compared to both TD children and children with GMFCS level I (Figs. 2 and 3). These results underscore the finding that children with increased motor impairment tend to have more altered muscle morphology.

Among all the knee extensors with decreased volume, only the rectus femoris was found to be shorter in children with GMFCS level II compared to TD children, and to children with GMFCS level I. This result is in accordance with the results of previous studies (Handsfield et al., 2016; Noble et al., 2014; Oberhofer et al., 2010). While it has been shown that knee extensors may decrease in strength when motor impairment increases in children with CP (Thompson et al., 2011), the current study's results showed that rectus femoris morphology might be particularly altered in children with GMFCS level II. It showed a large proportion of abnormal volumes (10/15) and lengths (9/15), which was less pronounced in children with GMFCS level I (Figs. 2 and 3).

The morphologies of the adductors (brevis, longus and magnus) and gracilis have been scarcely reported in the literature. In accordance with clinical examination-based data, the current study results showed a reduction in length of the gracilis and adductor longus. This reduction in length was more pronounced in children with GMFCS level II compared to I (Fig. 3).

Furthermore, children with GMFCS level II, with no previous orthopedic treatment, were not shown to significantly increase the volumes of their semimembranosus and semitendinosus with increasing age. In order to avoid further weakening of the hamstrings, which are known to be related to walking, jumping, and running abilities of children with CP (EeK and Beckung, 2008), it would be preferable to take the volumes of the hamstrings into account before any treatment is undertaken. Despite the increase in volume with age, rectus femoris, adductor longus, and biceps longus showed volumes that were shifted towards the lower limits of the 95% CI of the linear regression of TD children, with a higher percentage below this 95% CI noted in children with GMFCS level II compared to GMFCS level I (Fig. 4). This finding could underline the fact that factors influencing muscle growth, such as abnormal mechanical stimuli, growth factors (Gough and Shortland, 2012), or even early reduction of muscle size (Barber et al., 2011), could be more pronounced in children with GMFCS level II. This could account for the deterioration of these children's walking abilities during growth (Andersson and Mattsson, 2001).

A limitation of this study is its cross-sectional design, which limits conclusions related to the natural evolution of the morphology of the treatment-naïve proximal muscles in these children. However, a longitudinal study would be impossible because it would not be ethically feasible to refrain from treating children with CP. Another limitation of this study is the relatively small sample size, which was largely due to the stringent exclusion criteria related to the treatment history of these children and the difficulty to perform MRI exams on the lower limbs of infants due to the duration of acquisition during which children have to remain still. The mixture of hemiplegia and diplegia groups is also a limitation that could affect the interpretation of the results. Another source of error might be related to the visual identification of the muscle-tendon junction on the MRI images. Despite having strapped the patients to the MRI table at the level of lower limbs during the MRI acquisition, the difference in joint positions could have affected the muscle length results (Barber et al., 2011). Muscles of the shank were not studied because of the orthopedic treatment of 9/17 children with CP at this level; although treatment was performed at least one year prior to this study, we could not eliminate the effect of this treatment on pelvis and thigh

Although we may not be able to draw substantial conclusions due to some of the aforementioned limitations, nevertheless, these are the first results assessing the morphology and the growth of treatment-naïve pelvis and thigh muscles in children with CP, based on subject-specific 3D reconstructions.

5. Conclusion

The results of this study investigating the natural evolution of ambulant children with cerebral palsy confirm the assumption that morphological alterations of the pelvis and thigh muscles increase with the severity of motor impairment. Furthermore, volume growth alterations in children with GMFCS level II seem to be more pronounced compared to those with GMFCS level I. Muscle morphology was also found to be markedly heterogeneous in both children with GMFCS levels I and II, thus underlining the importance of a patient-specific approach for the treatment of these children. Patient-specific muscle treatment, taking into consideration the GMFCS level, and aiming to increase muscle size in children with CP, could help preserve or improve these children's motor functions during growth. This work is part of a larger project where subject-specific assessments of the musculoskeletal parameters of ambulant children with CP are being investigated. Future studies comparing dynamic muscle morphology during gait, while considering bone architecture, could help better understand the morphological and functional aspects of ambulant children with cerebral palsy with different GMFCS levels.

Conflict of interest

None.

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