ORIGINAL ARTICLE

Title: Effect of Low Dose Robotic-Gait Training on Walking Capacity in Children and Adolescents with Cerebral Palsy

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ABSTRACT

Objective: Robotic gait training presents a promising training modality. Nevertheless, evidence supporting the efficacy of such therapy in children with cerebral palsy remains insufficient. This study aimed to assess the effect of robotic gait training in children/adolescents with cerebral palsy.
Methods: Twenty-four children/adolescents with bilateral cerebral palsy (12 female, 10.1±3.1 years, Gross Motor Function Classification System II to IV) took part in this study. They received two 30-45 min sessions/week of Lokomat training for 12-weeks. Muscle strengths, 6-min walk exercise and gait parameters were evaluated pre- and post-training and at 6-months-follow-up. Training effect according to the level of impairment severity (moderate *vs* severe) was analyzed using a change from the baseline procedure.
Results: A significant increase in muscle strength was observed after training ($p \leq 0.01$). Hip flexors and knee extensors strength changes were maintained or improved at follow-up ($p < 0.05$). Comfortable walking speed was significantly increased by +20% after training with a slight reduction at follow-up compared to post-training condition (-2.7%, $p < 0.05$). A significant step length increase was observed after training (14%, $p \leq 0.001$). The distance covered in 6 min was higher in post-training (+24%, $p \leq 0.001$) and maintained at follow-up compared to pre-training conditions. No significant changes in kinematic patterns were observed. The analysis by subgroup showed that both groups of children (with moderate and severe impairments) improved muscle strength and walking capacities after Lokomat training.
Conclusion: The suggested Lokomat training induced improvement in walking capacity of children/adolescents with cerebral palsy whatever the level of severity. Hence, Lokomat training could be viewed as a valuable training modality in this population.

Keywords: Cerebral palsy, Gait analysis, Muscle strength, Robotic rehabilitation, Walking abilities

INTRODUCTION

Cerebral palsy (CP) is the leading cause of childhood gait limitations. Children with CP have varying degrees of muscle weakness, spasticity, bone deformities and impaired balance and coordination that limit their functional capacity to perform daily activities such as walking [4, 26]. These impairments cause a decline in gait capacities such as decrease in walking speed (due to a reduced step length and/or cadence), increase in double support duration, and poor endurance [15, 20, 30]. Because reduced walking speed and other gait abnormalities affect community integration and quality of life [37, 46], a priority of physical therapy interventions is to improve gait.

Over the past 2 decades, gait rehabilitation efforts have been extensively devoted to task-specific approaches with massive and intensive repetitions of the gait cycle to enhance neuroplasticity and to improve the potential for the recovery of walking after neurologic injury [36, 57]. In this context, some meta-analysis and systematic reviews highlighted that the locomotor treadmill training with partial body-weight support (BWS) leaded to positive effect on locomotor capacities of children with CP [8, 39, 41]. More precisely, the results of several studies [19, 27, 33] showed the advantage of locomotor treadmill training with BWS on muscle strength, walking speed, endurance and gait kinematics. Based on a similar approach, robotic-assisted gait training has become an increasingly common rehabilitation modality and has been purported as a potential approach for neuromotor-rehabilitation. Robotic rehabilitation is grounded on main principles of motor learning and neuroplasticity through mass practice and task-specific intervention to promote long-lasting neuromuscular adaptation [31, 32]. In this sense, the Lokomat, the most used walking robotic aid for gait rehabilitation, is totally adjustable in assistance (Guidance), BWS and velocity [47]. Lokomat training can be performed in a safe and playful way to maintain a high level of motivation and treatment adherence especially in pediatrics [38, 47]. However, the available evidence has not yet comprehensively highlighted the effectiveness of Lokomat training in different populations [35].

The current evidence about the clinical effectiveness and applicability of Lokomat training in pediatrics is weak [35]. In addition, contradictory results have been found concerning the effect of Lokomat training on gait capacities such as walking speed and walking endurance in children with CP. Borggraefe et al. [10, 11] highlighted a significant effect of Lokomat training (n=20, 12-sessions over 3-weeks) on gross motor performance measured by Gross Motor Function Measure 66-item scale (GMFM-66), walking speed, and walking endurance in children with CP. Later, Schroeder et al. [51] also reported a significant improvement in the GMFM-66 and patient's self-perception of performance after training (n=18, 12-sessions over 3-weeks), which was maintained at 8-weeks follow-up. However, in their study, walking speed and walking endurance were not significantly improved after the Lokomat training. In a retrospective study (n=67, at least one session/week), van Hedel et al. [25] reported a significant improvement in comfortable speed and function (measured by WeeFIM test) but no improvement in walking endurance and GMFM-66 was observed after Lokomat training. Lately, Wallard et al. [54, 55] highlighted a significant improvement in knee and ankle sagittal kinematics as well as dynamic balance control following Lokomat training combined with virtual reality in children who walk in jump gait (n=14, 20-sessions over 4-weeks). None of these studies has provided information on the effect of Lokomat training on lower limb muscle strength of children with CP. However, strength is a key parameter for locomotion given the strong relationship between muscle strength and walking ability in these children [3, 17, 21, 27]. Indeed, lower limb muscle strength explains approximately 21 to 47.8% of ambulatory capacities in children with CP [17, 23]. Moreover, the prescription employed across prior studies was very different, *i.e.* 2 to 12 weeks of gait training with a frequency of 1 to 5 sessions/week [11, 25, 54]. Despite the positive effects reported in previous studies, most studies used generic settings (*i.e.,* guidance, BWS and velocity) and their protocols were not or only partially reported.

Lokomat still requires further investigation to optimize routine clinical use. The disparate training schedules combined to the lack of information about Lokomat settings limit the understanding of the impact of Lokomat training on children with CP and may preclude the reproduction of the proposed protocols [2]. Future research should not only focus on “which therapeutic intervention could be superior to the other” but rather on how one type of therapy could be beneficial for a specific pathology, and a particular level of impairment severity (e.g., according to GMFCS levels). By including complete information on training description and settings it will be possible to gain specific knowledge on optimum way of using this robotic technology [2].

Based on this background, the present study aimed to assess the efficacy of Lokomat training to improve lower limb muscle strength, gait capacities and joint kinematics in children with bilateral CP with various impairments. We hypothesized that Lokomat training would increase lower limb muscle strength and locomotor capacities (*i.e.,* walking speed, step length and walking endurance), leading to a reorganization of the kinematics of walking. Furthermore, a secondary exploratory objective was to describe the training effect according to the level of impairment severity.

METHODS

Participants

Twenty-four children and adolescents with bilateral CP (age: 10.1±3.1 years, mass: 31.4±10.0 kg, height: 131.8±11.1 cm, sex: 12 Female) were included in this study (see **Table 1**).

The severity of motor impairment of participants was determined according to the GMFCS level (II (n=9), III (n=11) and IV (n=4)). The inclusion criteria were: (1) a diagnosis of spastic bilateral CP with a Gross Motor Function Classification System (GMFCS) level II to IV, (2) ability to communicate discomfort or pain, (3) understanding simple instructions, (4) ability to stand and walk without or with assistance, and (5) performing Lokomat training for the first time. The exclusion criteria were the presence of any contraindications to Lokomat training, botulinum toxin injections six months prior to the assessment, intrathecal baclofen pump or a surgical intervention during the last 12 months. All included participants received only Lokomat training during the study period, no additional physical therapy was provided. Motor impairment was considered moderate in children with GMFCS level II and severe in those with GMFCS level III and IV [44]. This study was approved by the Research Ethics Board of UHC Sainte-Justine.

Table.1 Demographic and clinical characteristics of participants

	Entire sample (n=24)	**GMFCS (II) (n=9)**	**GMFCS (III-IV) (n=15)**
Age (years)			
- Range	7-20	7-20	7-16
- Mean (SD)	10.1 (3.1)	10.3 (3.7)	9.9 (2.5)
Sex (F/M)	12/12	4/5	8/7
Mass (kg)	31.4 (10.0)	33.5 (9.9)	30.1 (9.6)
Height (cm)	131.8 (11.1)	134.5 (31.1)	130.5 (11.7)
Walking aids			
- None	8	8	-
- Canes	3	1*	2
- Walker	13	-	13

NOTE: *Assistive devices used for long distances.

Lokomat intervention

Gait training sessions were conducted at the Marie-Enfant rehabilitation center by experienced pediatric physical therapists using the Lokomat® Pro (version 5) with pediatric orthoses. The intervention consisted of 20-24 sessions of Lokomat training conducted over a 12-week period (2 sessions/ week, with at least one-day of rest between the training sessions). Each session started with a 5-minutes warm-up Lokomat walk with 100% Guidance and around 50% BWS and patient comfortable speed. The remaining time corresponded to Lokomat training with subject-specific settings. Throughout the training program, Lokomat settings were individually set according to the functional level of each patient. Guidance, BWS, and speed were gradually changed every 4-sessions according to children capacities. The BWS and Guidance force were adjusted for each patient as: 1) being superior to the minimum guidance and minimum BWS tolerated with keeping a functional walking, and 2) being inferior or equal to 50% of BWS. The speed was set to the maximum walking speed tolerated by the patient, and that which avoided an increase of spasticity that could interfere with the conduct of the Lokomat training sessions. Moreover, perceived exertion was evaluated at the end of each session using Borg scale in order to keep or adjust subject-specific settings [9]. When the session was perceived too difficult, a slight change in settings (e.g., decrease speed or increase Guidance) was made to allow the participant to perform at least 30 min of training. The Lokomat training was always combined with task-oriented exercises (e.g., step over an obstacle, kick a ball) and biofeedback to increase the patient 'motivation and promote their active participation.

Outcome measures

To assess the effectiveness of gait training, assessments were performed, immediately before (pre), after (post) training, and 6-months after the end of training (follow-up). Muscle strength was measured as *primary outcome measure*, and spatiotemporal parameters, endurance and kinematics were assessed as *secondary outcome measures*. Details about assessments are reported below.

Muscle strength

Before gait analysis, the *lower extremity strength* was assessed by an experienced using a hand-held dynamometer. The hand-held dynamometer allows a simple and an objective assessment of muscle strength and has a good intra-rater reliability for hip and knee flexor/extensor in children with CP (ICC = 0.77 – 0.96) [7, 16]. The positioning was defined in line with Eek et al. [22]. Children performed hip and knee maximal isometric voluntary contractions (three times each). They were asked to push "as hard and as fast as possible over" a 5-s period until hearing the auditory signal generated by the hand-held dynamometer. Three trials, followed by a 30-second rest period, were performed for each muscle group. The peak force reached during each trial was recorded by the hand-held dynamometer and the two closest values were averaged as recommended by [56].

Gait parameters

For each participant, a set of reflective markers were positioned on anatomical landmark based on the full body Plug-in Gait kinematic model [18]. A 12-camera motion capture system (T40x cameras, Vicon, Oxford, UK) was used to measure the 3D markers displacement with a sampling frequency of 100 Hz. Participants were asked to walk back and forth along a 12-m walkway at their self-selected speed. A 30-second rest period was provided after each 12-meter walk. Depending on impairment severity, two to four trials were correctly completed (i.e., continuous walking without stopping or losing markers). Between two and twelve gait cycles were averaged to compute kinematic data. The data were further analyzed with a customized Matlab program (MathWorks Inc., Natick, MA, USA) to obtain spatiotemporal gait parameters: walking speed, cadence, stride length, and percent time spent in single and double support; and sagittal joint kinematic gait parameters: pelvis, hip, knee and ankle minimum and maximum angles as well as range of motion (ROM) during the stance phase.

Walking endurance

To assess changes in *walking endurance*, a 6-minutes walking test (6mwt) was performed after the gait analysis. The participants were asked to walk continuously at their comfortable self-selected speed for 6-minutes which is considered as representative of possible daily walking distances [12, 45]. In line with Brehm et al.'[12], our instructions were to walk continuously at comfortable speed without stopping or resting. Standardized encouragements were provided [12, 45].

Statistical analysis

Normality of the distribution was determined using the Lilliefors test. According to the normality of the distribution, the mean (± standard deviation) or the median (percentiles: 25th–75th) was displayed as descriptive statistics. To assess the efficacy of Lokomat training, a linear mixed model (LMM) was used to compare pre, post and follow-up evaluations. P-values were corrected with false discovery rate (FDR) procedure for multiple comparisons (q fixed at 0.10; FDR=10%) [6]. In case of significance, Tukey post-hoc tests were performed to identify evaluation periods (pre, post, follow-up) that were significantly different from each other. In order to explore the training effect according to the level of impairment severity, a change from the baseline procedure (difference between pre and post results) was used to compare the changes in the groups (moderate *vs* severe) using Mann-Whitney test. As it is recognized that there are large inter-limb differences in children with CP, analysis considered each side independently (n=2×24), as done in previous studies [13, 48, 49]. All statistical analyses were executed using R software (R 3.6.0, RCore Team 2019).

RESULTS

Training parameters

Overall, all participants completed pre and post training assessments. However, only 19 out of 24 participants completed follow up assessments. Due to lack of availability, 3 out of these 19 children completed the follow-up assessment 9-12 months after the end of training (instead of 6 months).

The Lokomat settings of each subject are reported in Appendix A. The walking distance evolved from 444.5±148.8 m at the beginning to 1268.5±174.5 m at the end of training. The BWS was set on average to 47.4±7.4% at the beginning and was progressively reduced to reach 21.6±9.3% at the end of the training. The average of guidance progressed from 100% at the beginning to 64.5±14.5% at the end of Lokomat training. Treadmill speed was increased by 49% (from 1.2 ±0.14 km/h to 1.8±0.23 km/h) over the training.

Effect of training on muscle strength and walking capacities

Muscle strength

After Lokomat training, significant improvement in muscle strength was observed (Table 2). The increase varied by 25% and 74% for hip flexors (mean change = 6.4±7.1 Nm) and extensors (mean change = 7.1±11.0 Nm) strength respectively (p=0.0001) and by 35% and 32% for knee flexors (mean change = 4.8±6.0 Nm) and extensors strength (mean change = 7.0±7.5 Nm) (p=0.0001). These changes in muscle strength were maintained or improved during follow-up.

Table.2 Muscle strength outcomes in pre-, post and follow-up tests. Values are expressed as means (SD). (p critical value = 0.05, q = 10%)

	Muscle strength (Nm)			**LMM**	**Post-hoc tests**		
Muscle group	**Pre**	**Post**	**Follow-up**	**p-value**	**Pre vs Post**	**Pre vs F.up**	**Post vs F. up**
Hip flexors	25.2 (16.2)	31.5 (16.4)	35.7 (19.4)	**<0.0001**	**<0.0001**	**<0.0001**	**0.0027**
Hip extensors	9.6 (10.5)	16.7 (18.0)	19.9 (18.3)	**<0.0001**	**<0.0001**	**<0.0001**	0.8722
Knee flexors	13.7 (9.6)	18.5 (11.1)	19.1 (12.5)	**<0.0001**	**<0.0001**	**<0.0001**	0.9276
Knee extensors	21.7 (12.7)	28.6 (11.9)	32.0 (14.7)	**<0.0001**	**<0.0001**	**<0.0001**	**0.0183**

NOTE: LMM means Linear Mixed Model. Significant p-values are mentioned in bold.

Gait parameters

The gait parameters were divided into two categories (i) Gait capacities including walking speed, step length, cadence, the single and double support time and walking endurance (Table.2) and (ii) Sagittal lower limb kinematic in sagittal plane (Table.3 & Figure.1).

Concerning gait capacities, a significant increase in walking speed was observed in post-test (mean change = 0.12±0.14 m/s, relative change = 20%, $p<0.001$) and showed a slight but significant reduction at follow-up (mean change = 0.04±0.33 m/s, relative change = -2.7%, $p<0.05$), resulting in a global significative improvement (Follow-up vs pre-test) of 18% (mean change = 0.13±0.34 m/s). This increase in walking speed was the result of a significant increase in step length (mean change = 0.06±0.09 m, relative change = 14%, $p<0.001$) in post-test. No significant changes were observed in cadence, single and double support time after training. A significant improvement in walking endurance was observed in post-test (mean change = 47.8±33.69 m, relative change = 24%, $p<0.0001$) and maintained at follow-up ($p<0.01$).

Table.3 Walking capacities and kinematics outcomes in pre-, post and follow-up tests. (p critical value=0.05, q=10%)

	Assessments			**LMM**	**Post-hoc tests**		
	Pre (n=24)	**Post (n=24)**	**Follow-up (n=19)**	**p-value**	**Pre vs Post**	**Pre vs F.up**	**Post vs F.up**
Walking capacities							
Speed (m/s)	0.62 (0.26)	0.75 (0.26)	0.73 (0.28)	**<0.0001**	**<0.0001**	**0.0188**	**0.0214**
Step length (m)	0.37 (0.10)	0.42 (0.11)	0.40 (0.10)	**0.0019**	**0.0007**	0.3204	**0.0339**
Cadence (step/min)	98 (28.2)	103 (27.0)	105 (29.0)	0.2348	-	-	-
Single support (%)	35.1 (7.5)	37.2 (7.1)	35.1 (7.3)	*0.0997*	-	-	-
Double support duration (%)	50.7 (4.8)	50.3 (3.9)	50.3 (4.0)	0.7862	-	-	-
Endurance-6mwt (m)	197 (109-311)	245 (182-356)	242 (188-319)	**0.0005**	**<0.0001**	**0.0025**	0.5670
Lower limb kinematic							
Pelvis ante/retroversion (˚)							
- ROM in stance	5.8 (3.5)	6.7 (3.6)	6.3 (3.5)	0.1272	-	-	-
- Peak anteversion at stance	23.0 (8.4)	21.5 (7.9)	21.4 (9.4)	0.2455	-	-	-
- Peak retroversion at stance	17.2 (8.5)	14.7(8.1)	15.1(9.5)	0.1107	-	-	-
Hip Flexion/Extension (˚)							
- ROM in stance	41.8 (9.4)	43.6 (9.3)	41.9 (8.3)	0.3514	-	-	-
- Peak flexion at stance	46.7 (11.5)	46.4 (12.4)	45.0 (12.3)	0.8461	-	-	-
- Peak extension at stance	5.0 (11.4)	2.8 (13.0)	3.1 (12.2)	*0.0808*	-	-	-
- Angle at initial contact	25.7 (24.2)	25.3 (24.4)	24.6 (23.6)	0.9812	-	-	-
- Peak extension at single support	7.1 (12.0)	4.6 (13.0)	4.6 (12.5)	**0.0374**	0.0607	0.9930	0.0735
Knee Flexion/Extension (˚)							
- ROM in stance	25.0 (11.1)	25.1 (9.3)	28.5 (10.4)	0.5921	-	-	-
- Peak flexion at stance	39.6 (13.4)	40.7 (12.9)	41.9 (13.3)	*0.0932*	-	-	-
- Peak extension at stance	14.6 (17.4)	15.6 (17.2)	13.4 (17.5)	0.4072	-	-	-
- Angle at initial contact	25.2 (17.6)	26.0 (17.8)	25.2 (18.5)	0.5547	-	-	-
- Peak extension at single support	15.1 (17.6)	16.0 (17.5)	15.2 (17.6)	0.4788	-	-	-
Ankle Flexion/Extension (˚)							
- ROM in stance	20.0 (9.0)	22.2 (11.8)	22.7 (8.6)	0.5686	-	-	-
- Peak dorsi-flexion at stance	15.4 (11.8)	15.5 (13.1)	14.0 (11.9)	0.4847	-	-	-
- Peak plantar-flexion at stance	-3.9 (11.3)	-6.7 (10.2)	-8.7 (14.8)	0.2043	-	-	-
- Angle at initial contact	4.0 (16.3)	4.6 (15.1)	5.2 (14.0)	0.7750	-	-	-

NOTE: LMM means Linear Mixed Model. Significant p-values are mentioned in **bold.** Values are expressed as means (SD). Endurance data are not normal. Endurance values are given as medians (percentiles: 25th-75th).

Regarding lower limb kinematic, a main effect of training was observed in hip extension angle during single support (p=0.04). We also observed a tendency on maximal hip extension (p=0.08) as well as maximal knee flexion (p=0.09) during the stance phase. However, Post-hoc tests were not significantly different when comparing the pre, post and follow-up data (Table.3).

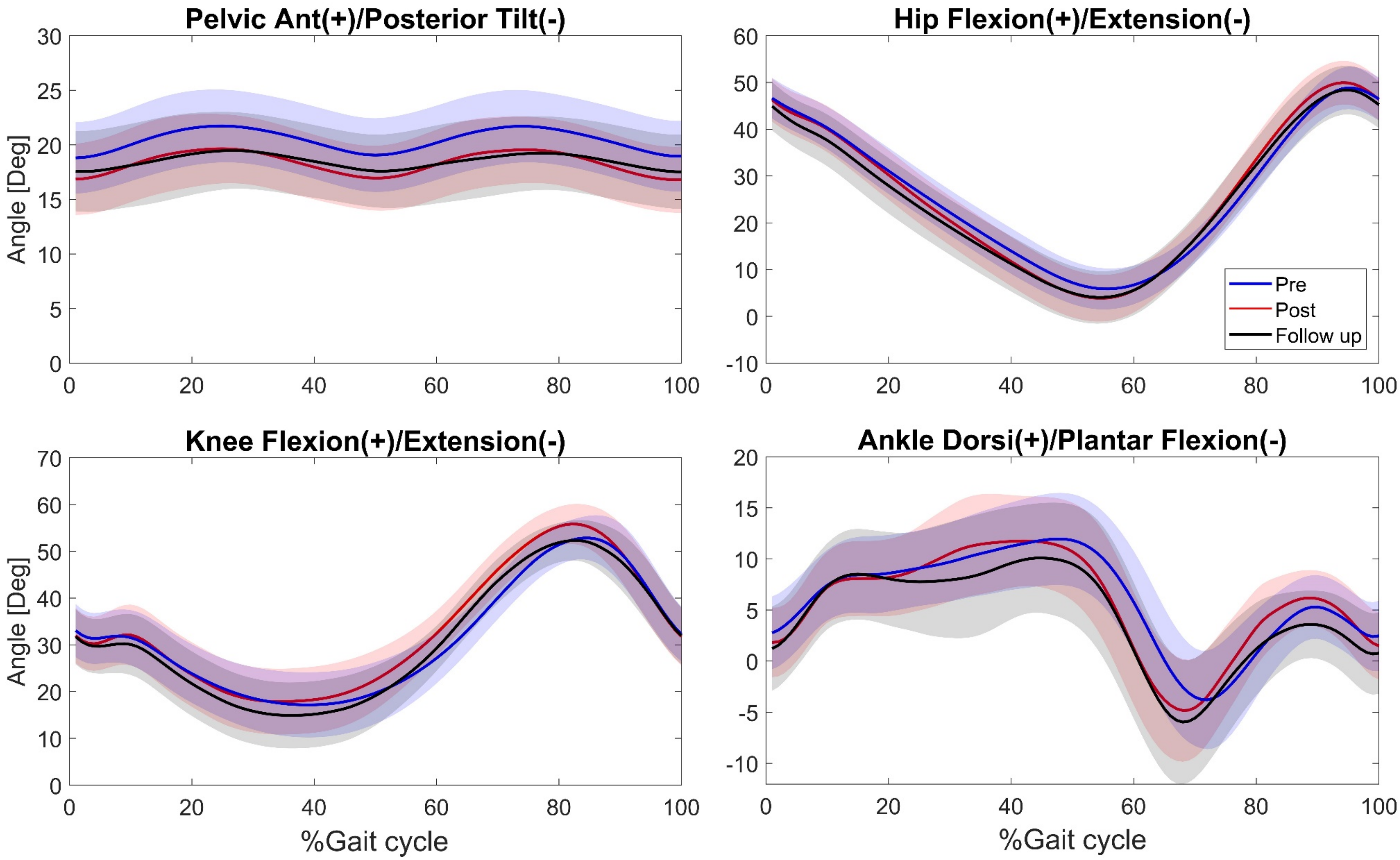

Figure.1 Sagittal kinematic at pre-training (blue line), post-training (red line) and follow-up (black line) in children with bilateral CP. Shaded region denotes 95% confidence interval in each condition.

Effect of training according to impairment severity

Following the analysis by sub-group, both groups (moderate and severe impairments) showed a significant improvement in muscle strength (Figures.2) as well as in most of gait capacities (Figure.3 and Appendix.B). In children with moderate impairment, the increase in muscle strength varied by 19% (mean change = 6.2±5.8 Nm) and 65% (mean change = 10.3±12.2 Nm) in hip flexors and extensors respectively and by 32% (mean change = 5.4±5.5 Nm) and 27% (mean change = 7.0±5.5 Nm) in knee flexors and extensors. In the group with severe impairment, hip flexors and extensors increased by 31% (mean change = 6.4±7.7 Nm) and 91% (mean change = 5.3±9.7 Nm) and knee flexors and extensors increased by 38% (mean change = 4.4±6.1 Nm) and 36% (mean change = 6.9±8.4 Nm). Concerning gait capacities, walking speed, step length, and walking endurance increased by 11% (mean change = 0.10±0.13 m/s), 10% (mean change = 0.04±0.06 m) and 18% (mean change = 56.1±28.7 m) in children with moderate impairment and from 30% (mean change = 0.14±0.14 m/s), 18% (mean change = 0.06±0.10 m) and 34% (mean change = 42.9±34.3 m) in children with severe impairment. However, the change from the baseline was not significantly different between the two groups in all parameters ($p > 0.05$, Table.4). No significant change was observed in sagittal joints ROM for the two groups.

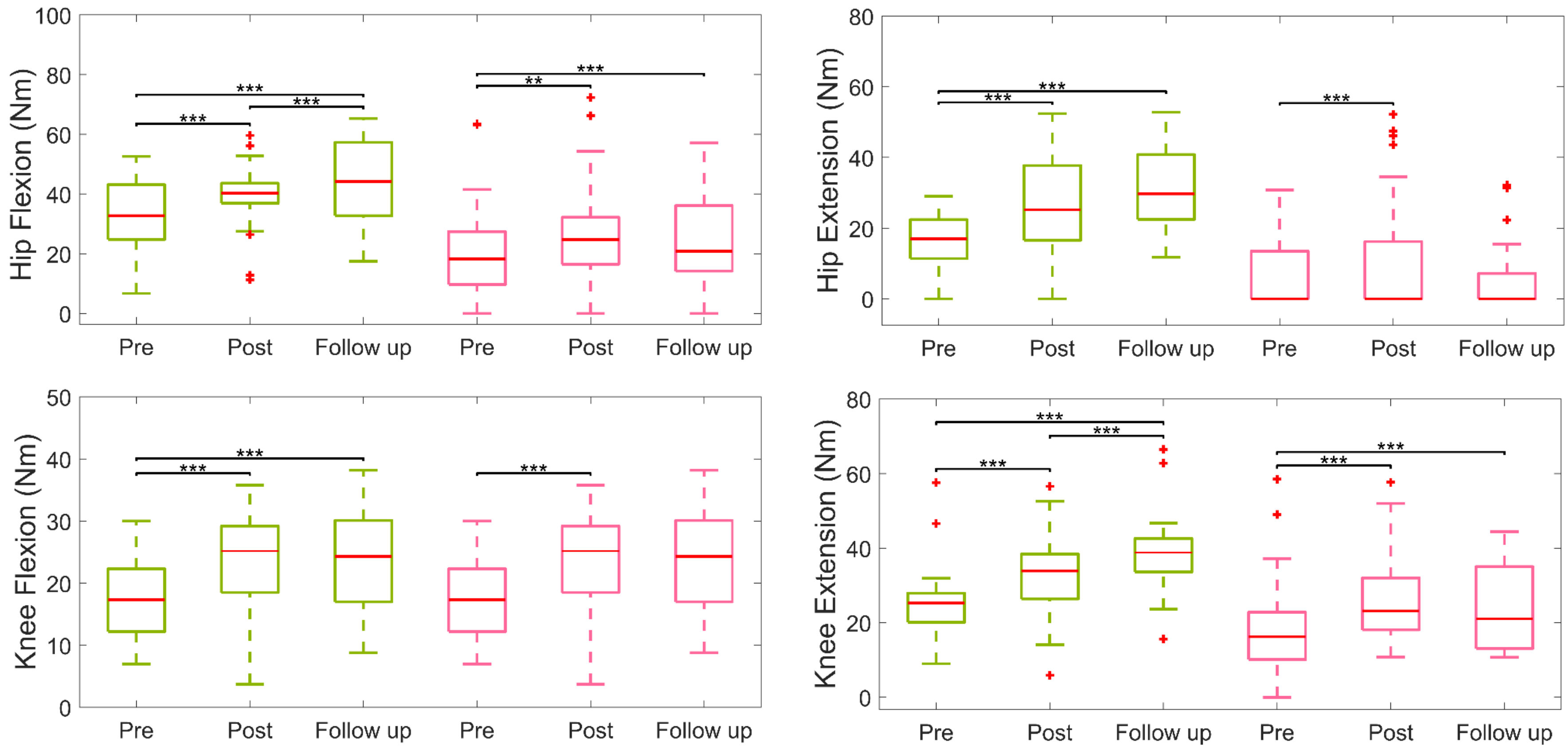

Figure.2 Lower limb muscle strengths at pre, post and follow-up in children with moderate impairment (in green) *vs.* children with severe impairment (in pink). Asterisks represent significance (*$p \leq 0.05$; **$p \leq 0.01$, ***$p \leq 0.001$).

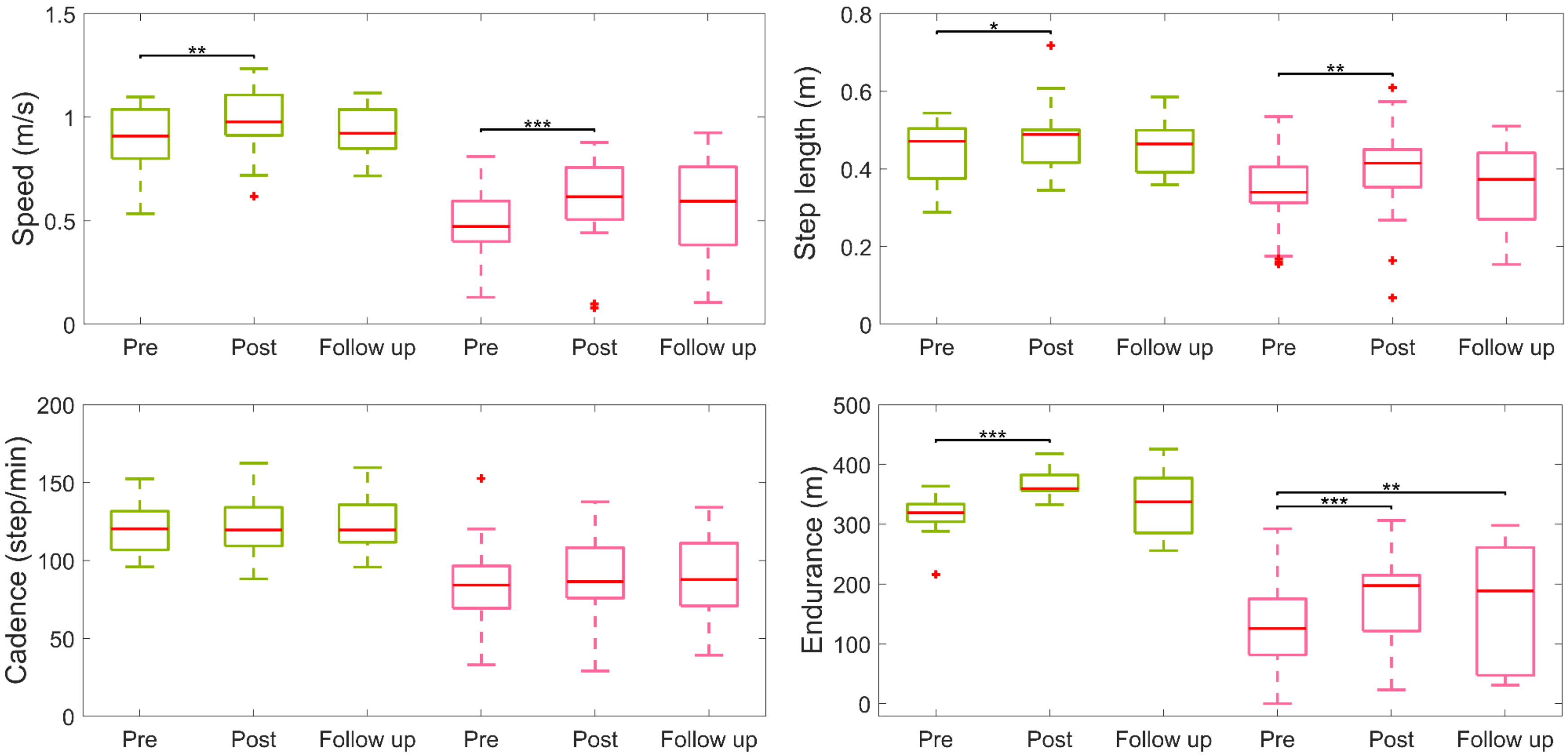

Figure.3 Gait capacities at pre, post and follow-up in children with moderate impairment (in green) *vs.* children with severe impairment (in pink). Asterisks represent significance (*$p \leq 0.05$; **$p \leq 0.01$, ***$p \leq 0.001$).

Table.4 Change from Baseline over time (change between Post-training and Pre-training) in lower limb muscle strength and walking capacities in children with moderate (GMFCS II) and severe (GMFCS III-IV) impairments. Data are not normal. Value are given as medians (percentiles: 25th-75th).

Parameters	Change form baseline GMFCS (II)	Change form baseline GMFCS (III-IV)	p-value
Hip flexors (N.m)	7.7 (1.3-9.5)	5.1 (0.7-10.5)	0.881
Hip extensors (N.m)	6.8 (0.4-22.9)	0.0 (0.0-6.0)	0.133
Knee flexors (N.m)	5.9 (4.9-8.4)	4.9 (0.0-9.2)	0.655
Knee extensors (N.m)	6.6 (2.5-11.0)	6.8 (0.8-13.9)	0.741
Speed (m/s)	0.09 (0.04-0.20)	0.14 (0.02-0.26)	0.482
Step length (m)	0.02 (0.0-0.09)	0.05 (0.01-0.11)	0.338
Endurance (m)	58.0 (34.8-71.4)	26.8 (21.9-68.7)	0.653

DISCUSSION

The objective of this study was to assess the effect of a robotic gait training in children and adolescents with CP while detailing the training program to facilitate its clinical application. The main finding of the present study was that following our Lokomat training protocol, the group of children with CP improved their gait capacities as well as their lower limb muscle strength (*i.e.,* walking speed, step length, endurance). The improvements in endurance and muscle strength were maintained at follow-up. The second finding was that both groups of children (with moderate and severe impairments) improved muscle strength and walking capacities after Lokomat training.

Intervention and progress in settings

The optimal training frequency and duration for gait rehabilitation with the Lokomat remains questionable because of the large variability between protocols in previous studies. In the present study, we made the choice to put in place a protocol of intervention with 2 sessions/week for 12 weeks with a gradual increase in intensity. According to the recommendations of Verschuren et al., (2016), longer interventions with progressive intensities (*e.g.,* duration: 8–16 weeks; frequency: 2 or 4 sessions/week) may be needed to experience meaningful motor function improvements in in children with CP. Our training frequency and duration choices meet those recommendations. Furthermore, our training frequency (2 sessions/week) was adapted to the availabilities of children and their parents which allows a fast translation to clinical environment. Since, most of participants in this study attend either special education, involving time-consuming door-to-door transportation, or mainstream education, which can be demanding, cause burden, and limit time for training. These factors were highlighted as an important barriers of participation in this population [5, 28]. Although not proven to be optimal, an intervention of two sessions/week for 12 weeks is effective and possible to be implemented in clinics with school children with CP.

Concerning the progression in Lokomat settings, it has been suggested that, in order to get closer to the normative gait patterns, very low speeds and high levels of BWS should be avoided when possible [14, 29]. The initial BWS and treadmill speed were adjusted according to these recommendations. Then, the progression in these parameters was mainly based on patient fatigability using Borg scale [9]. This approach worked well since BWS was decreased by 53% (from 47.4±7.4% to 21.6±9.3%) and the treadmill speed was increased by 49% (from 1.2 ± 0.14 km/h to 1.8 ± 0.23 km/h). The progression in BWS was slightly higher in our study than that reported by Wallard et al., (2017) (BWS decreased by 43% from 70% to 40%). The change in treadmill speed was lower in our study (49%) compared to Wallard et al., (2017) (speed increased by 100% from the 0.7 km/h for all participants to 1.4 km/h). Since, we started at higher initial speed. This may denote a better initial evaluation and personalization of this setting in our study. The role of the guidance is less obvious than walking speed and BWS. Since recommendations for setting the guidance is to use low guidance level to promote active patient participation, we adjusted this parameter depending on the locomotor capabilities of the patient and to ensure a functional walking (e.g., alternate well the steps, feet do not trip, etc). The guidance was reduced from 100% to 64.5% at the end of training. Overall, our evaluation routine (every 2 weeks) allowed an important, gradual and personalized progression in Lokomat settings. Finally, the experience and judgment of the therapist remains a key factor to better personalize and better adjust the settings of the Lokomat [40].

Effect of training on muscle strength and walking capacities

There is a strong relationship between muscle strength and walking abilities in children with CP [3, 17, 21]. After our Lokomat training, the group of children with CP had a significant improvement in their lower extremity strength (25-74%) combined with an improvement in locomotor parameters (*i.e.,* walking speed (+20%), step length (+14%) and endurance (+24%)). The improvement in endurance was maintained over time. Overall, the improvement in muscle strength (14-16 out of 24 children) exceeds the minimal detectable change in children with CP (minimal detectable change: 20.6-24.7% [56]). Concerning walking capacities,14 out of 24 children had change in their walking speed greater than the minimal clinically important difference (0.1 m/s; [43]), and 10 had a change in their walking endurance that was above the minimal clinically difference (54.9 m; [52]). These walking capacities may reflect exercise tolerance required for the performance and predict ability to walk in the community. In prior studies [1, 42], the specific strength training showed a significant improvement in muscle strength but not accompanied by an increase in any locomotor parameters such as walking speed or stride length, and inconclusive evidence regarding improvements in gross motor function. In Scholtes et al. (2010)'s randomly controlled study (n=51 children with CP), a 12-weeks of progressive strength training did not lead to improved locomotor parameters [50]. Compared to these latest studies, our functional gait training leads to an improvement in muscle strength similar than strength training and an improvements in gait capacities such as walking speed, step length and endurance which are of utmost importance for the community participation and integration in children with CP (LaPlante & Kaeser, 2007; Pirpiris et al., 2006). Additional information about the patient's daily life-based gait performance, as a complement to laboratory-based assessments, could improve the understanding of the patient's overall gait difficulties, enhancing clinical care.

Effect of training according to impairment severity

It has been shown that children and adolescents with a GMFCS level of I and II show similar developmental curves differing notably from those of patients with a GMFCS level of III and IV [24]. By investigating the benefit of robotic rehabilitation according to the GMFCS levels, our results highlighted a significant improvement in muscle strength, walking speed, step length and endurance in children with moderate impairment (GMFCS level II) as well as the children with severe impairment (GMFCS levels III-IV). Despite the relative changes (%) which are greater in the group with severe impairment, the changes from the baseline were not statistically different between these two groups. These results are dissimilar to the results of Hedel et al. (2016) who suggest that children with severe impairment (GMFCS III-IV, n=52) may benefit more from the Lokomat training than children with moderate impairment (GMFCS II, n=15). In their study, children with GMFCS II level did not have any significant improvement in terms of mobility (measured by WeeFIM), walking speed and endurance. However, as in their study participants received Lokomat training in complement to conventional therapies, it was difficult to determine the extent of improvements in walking-related outcomes caused by Lokomat only. Our current results highlighted that Lokomat training has positive effect on muscle strength and gait capacities (*i.e.,* walking speed, step length and endurance) whatever the level of severity (from GMFCS levels II to IV).

Lack of change in lower limb range of motion

Our results did not show any significant changes in sagittal lower limb range of motion. The trend of changes in the hip extension (p=0.08) and knee flexion (p=0.09) peaks at stance phase suggest potentially that two training sessions per week were not enough to drive a significant change in lower limb range of motion of children with CP. In addition, the heterogeneity of the participant gait patterns present in our sample could partly explain the absence of significant effect on joint kinematics. With a more intense training (5 sessions per week) including a homogeneous gait pattern (only children with CP who walk in jump gait), Wallard et al., [54] reported significant improvement in joint kinematics after Lokomat training. However, this study was based on a very intense training frequency (5 sessions per week) which not possible to apply in our case. A training frequency of 5 sessions per week requires that the patient be followed internally if not it would imply a huge investment in terms of time and effort for children who go to school and their parents. However, it should be mentioned that the intensity of the training is part of the principles of neuroplasticity to promote learning [32]. Higher training intensity is needed to induce neuroplasticity and promote motor learning.

Study limitations

There are some limitations of this present study that need to be considered. Firstly, the heterogeneity of our sample which could alter our results. However, it reflects the clinical patient population of a pediatric rehabilitation center well. Secondly, for reasons of health, geography or disinterest, five children dropped out of the follow-up assessments. Furthermore, the therapies during follow up were not standardized. While a few participants received one session of general physiotherapy per week, others did not receive any therapy since it was during summer vacation period. Thirdly, as the limitation of several previous studies [10, 11, 25], the present study did not include neither a control group receiving no therapy at all nor a control group receiving conventional therapy. Then, we cannot exclude the natural progression of gait function in children with CP on our findings. Moreover, we cannot conclude that Lokomat training was superior to conventional therapy. Fourthly, muscle strength was measured during isometric muscle contractions, which is not task-specific to walking movement [13]. Fifthly, the difficulty of training was subjectively judged by the therapist based in his experience and by asking the patient about his perception of exertion. A combination with a heart rate monitor would have been a better alternative to ensure an objective monitoring of training difficulty.Sixthly, the absence of difference in change between the two groups in our study could be due to the small sample size in the two groups. Finally, in the present study, we reported several lab-based walking capacities measures including 3D gait analysis which serve clinical decision making. A perspective will be to monitor also the day-to-day ambulatory activity to determine how the gain in walking speed and endurance are transferred to daily-life activities.

CONCLUSION

In summary, a 2-sessions per week Lokomat training for 12 weeks results in a significant improvement of endurance, walking speed and step length, as well as, lower limb muscle strength. This training program was easily performed in children and adolescents with CP without any undesirable side effects. Hence, Lokomat is an interesting modality for locomotor training in children with CP with a GMFCS levels II to IV.

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Disclosure statement

The authors declare that they have no competing interest.

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APPENDICES

Appendix A. Changes in Lokomat settings between the first and the last training sessions

	Distance (m)		Guidance (%)		BWS (%)		Speed	
	Initial	**Final**	**Initial**	**Final**	**Initial**	**Final**	**Initial**	**Final**
P1	610	1369	100	44	36	14	1.3	1.7
P2	585	1470	100	78	53	21	1.3	2.0
P3	648	1156	100	71	32	24	1.2	1.6
P4	641	1004	100	84	65	34	1.1	1.8
P5	748	1273	100	67	47	14	1.3	1.6
P6	687	1261	100	75	50	17	1.2	1.4
P7	450	1200	100	50	43	21	1.0	1.8
P8	283	1267	100	72	48	31	1.3	1.9
P9	445	1178	100	79	58	22	1.4	1.9
P10	492	1444	100	49	40	12	1.5	1.8
P11	400	1250	100	70	47	19	1.2	1.7
P12	583	1403	100	48	38	11	1.4	1.8
P13	450	1100	100	60	47	33	1.3	1.6
P14	450	1000	100	40	38	15	1.0	1.7
P15	436	1216	100	47	41	14	1.3	1.6
P16	450	1272	100	83	48	37	1.2	1.7
P17	300	1500	100	85	54	21	1.0	2.0
P18	321	1549	100	51	48	26	1.3	2.1
P19	290	1200	100	50	54	16	1.2	2.3
P20	300	1300	100	80	54	16	1.2	2
P21	300	1633	100	50	48	11	1.5	2.3
P22	300	1000	100	60	50	26	1.2	1.6
P23	200	1000	100	75	54	49	1.1	1.9
P24	300	1400	100	80	44	12	1.4	2.2
Mean	444.5	1268.5	100.0	64.5	47.4	21.6	1.2	1.8
SD	148.8	174.6	0.0	14.5	7.4	9.3	0.1	0.2

Appendix B. Changes in muscle strength and walking capacities after training in function of GMFCS level. Data are not normal. Value are given as medians (percentiles: 25th-75th)

	Pre	Post	Follow-up	LMM results	Pre vs Post	Pre vs F.up	Post vs F.up
Muscle strength							
Hip flexors (N.m)							
- GMFCS II	32.7 (24.8-43.1)	40.2 (36.9-43.6)	44.1 (32.7-57.3)	**0.0001**	**0.0002**	**0.0001**	**0.0008**
- GMFCS III-IV	18.2 (9.7-27.4)	27.2 (16.5-32.0)	20.8 (14.2-36.1)	**0.0001**	**0.0001**	**0.0001**	0.4139
Hip extensors (N.m)							
- GMFCS II	16.9 (11.4-22.4)	25.2 (16.6-37.7)	29.7 (22.5-40.8)	**0.0001**	**0.0007**	**0.0001**	0.2390
- GMFCS III-IV	0.0 (0-13.5)	0.0 (0-16.2)	0.0 (0-7.2)	**0.0018**	**0.0005**	0.4125	0.1330
Knee flexors (N.m)							
- GMFCS II	17.3 (12.2-22.3)	25.1 (18.5-29.2)	24.3 (17.0-30.1)	**0.0001**	**0.0001**	**0.0001**	0.8717
- GMFCS III-IV	8.4 (3.2-18.9)	14.8 (8.8-19.9)	9.3 (3.6-20.8)	**0.0025**	**0.0009**	0.1000	0.5639
Knee extensors (N.m)							
- GMFCS II	25.2 (20.1-27.9)	33.9 (26.4-38.4)	38.9 (33.6-42.6)	**0.0001**	**0.0001**	**0.0001**	**0.0001**
- GMFCS III-IV	16.2 (10.1-22.8)	23.1 (18.1-32.0)	21.0 (13.1-35.0)	**0.0001**	**0.0001**	**0.0001**	0.9904
Gait parameters							
Speed (m/s)							
- GMFCS II	0.91 (0.80-1.04)	0.98 (0.91-1.1)	0.92 (0.84-1.0)	**0.0045**	**0.0014**	0.1828	0.1925
- GMFCS III-IV	0.47 (0.40-0.60)	0.61 (0.51-0.75)	0.59 (0.38-0.7)	**0.0006**	**0.0001**	0.1190	0.0953
Step length (m)							
- GMFCS II	0.47 (0.37-0.50)	0.49 (0.42-0.50)	0.46 (0.39-0.50)	**0.0267**	**0.0147**	0.2199	0.4984
- GMFCS III-IV	0.34 (0.31-0.40)	0.41 (0.35-0.45)	0.37 (0.27-0.44)	**0.0046**	**0.0023**	0.6680	0.1032
Cadence (step/min)							
- GMFCS II	120.3 (106.8-131.6)	119.5 (109.3-134.1)	119.5 (111.7-135.7)	0.8101	-	-	-
- GMFCS III-IV	84.2 (69.2-96.5)	86.4 (75.9-108.2)	87.7 (70.9-111.1)	0.2528	-	-	-
Endurance (m)							
- GMFCS II	319.3 (304.2-333.5)	359.6 (356.0-382.1)	337.4 (285.4-377.2)	**0.0084**	**0.0012**	0.3545	0.0801
- GMFCS III-IV	125.8 (81.4-175.0)	197.2 (121.5-214.8)	188.6 (47.3-261.0)	**0.0016**	**0.0013**	**0.0016**	0.9013

NOTE: LMM means Linear Mixed Model. Significant p-values are mentioned in **bold**.