ACRM
AMERICAN CONGRESS OF REHABILITATION MEDICINE

Archives of Physical Medicine and Rehabilitation

journal homepage: www.archives-pmr.org

Archives of Physical Medicine and Rehabilitation 2020;101:106-12

ORIGINAL RESEARCH

Effect of Robot-Assisted Gait Training in a Large Population of Children With Motor Impairment Due to Cerebral Palsy or Acquired Brain Injury

Elena Beretta, MD,[a] Fabio Alexander Storm, PhD,[b] Sandra Strazzer, MD,[a] Flaminia Frascarelli, MD,[c] Maurizio Petrarca, PhD,[c] Alessandra Colazza, PT,[c] Giampietro Cordone, PT,[c] Emilia Biffi, PhD,[b] Roberta Morganti, PT,[b] Cristina Maghini, MD,[d] Luigi Piccinini, MD,[d] Gianluigi Reni, Eng,[b] Enrico Castelli, MD[c]

From the [a]Scientific Institute, IRCCS "E. Medea," Acquired Brain Injury Unit, Bosisio Parini, Lecco; [b]Scientific Institute, IRCCS "E. Medea," Bioengineering Laboratory, Bosisio Parini, Lecco; [c]Bambino Gesù Children's Hospital, Neurorehabilitation Units, Rome; and [d]Scientific Institute, IRCCS "E. Medea", Functional Rehabilitation Unit, Bosisio Parini, Lecco, Italy.

Abstract

Objective: To evaluate retrospectively the effect of robotic rehabilitation in a large group of children with motor impairment; an additional goal was to identify the effects in children with cerebral palsy (CP) and acquired brain injury (ABI) and with different levels of motor impairment according to the Gross Motor Function Classification System. Finally, we examined the effect of time elapsed from injury on children's functions.

Design: A cohort, pretest-posttest retrospective study was conducted.

Setting: Hospitalized care.

Participants: A total of 182 children, 110 with ABI and 72 with CP and with Gross Motor Function Classification System (GMFCS) levels I-IV, were evaluated retrospectively.

Interventions: Patients underwent a combined treatment of robot-assisted gait training and physical therapy.

Main Outcome Measures: All the patients were evaluated before and after the training using the 6-minute walk test and the Gross Motor Function Measure. A linear mixed model with 3 fixed factors and 1 random factor was used to evaluate improvements.

Results: The 6-minute walk test showed improvement in the whole group and in both ABI and CP. The Gross Motor Function Measure showed improvement in the whole group and in the patients with ABI but not in children with CP. The GMFCS analysis showed that all outcomes improved significantly in all classes within the ABI subgroup, whereas improvements were significant only for GMFCS III in children with CP.

Conclusions: Children with motor impairment can benefit from a combination of robotic rehabilitation and physical therapy. Our data suggest positive results for the whole group and substantial differences between ABI and CP subgroups, with better results for children with ABI, that seem to be consistently related to time elapsed from injury.

Archives of Physical Medicine and Rehabilitation 2020;101:106-12

The improvement of walking ability is one of the primary rehabilitation goals for children with neurologic impairment. Gait training is a key component of pediatric rehabilitation and one of the major challenges for rehabilitation specialists. Parents often give walking as a main goal for their children, focusing predominantly on normal gait pattern, gait quality, and independence.

In pediatric ages, the most frequent groups of neuromotor disorders with impairment of walking are cerebral palsy (CP) and acquired brain injury (ABI). CP describes a group of permanent disorders of the development of movement and posture causing activity limitation, that are attributed to nonprogressive

Supported by a private donation through "Associazione La Nostra Famiglia" and by the Italian Ministry of Health (Ricerca Corrente 2017/2018/2019 to Eng G. Reni). Bambino Gesù Children's Hospital thanks "Fondazione Roma" for the generous contribution to the purchase of the Lokomat robotic system.

Clinical Trial Registration No.: NCT03828110.

Disclosures: none.

0003-9993/19/$36 - see front matter © 2019 by the American Congress of Rehabilitation Medicine

https://doi.org/10.1016/j.apmr.2019.08.479

disturbances that occurred in the developing fetal or infant brain.[1] CP is the most frequent cause of motor, sensory, and cognitive disability in childhood: its incidence is 2 per 1000 live births.[2]

ABI is the leading cause of death and neurologic disability in children after infancy.[3] The term refers to a brain injury sustained after a period of normal development. Functional impairments (motor, behavioral, educational, cognitive) are common and can endure for years after ABI.[4,5]

Until now, combinations of physiotherapy and orthopedic and medical interventions have been the mainstay for the recovery of gait in children with gait impairment.[6,7] In the last few years, traditional treatments have been combined with innovative therapies, such as robot-assisted gait training (RAGT), which has emerged as a new interesting rehabilitation tool for patients with neurologic impairment.[8]

RAGT can provide controlled, intensive, task-specific training that is goal directed and cognitively engaging. These aspects, together with the repetition of steps, promotes a physiological-like movement of limbs able to enhance neuroplasticity and to improve the potential for the recovery of walking after neurologic injury.[9,10]

Compared with standard interventions, motivation during RAGT may be greater for children because they are often both accustomed to and interested in technology.[11] Interest and enhanced tolerability may increase practice time and reduce overall treatment durations.[12]

RAGT provides optimal difficulty level with variable degrees of body weight support and guidance force.[13] This allows a personalization of the intervention in line with the patient's abilities.[14]

The majority of the available data supporting the effectiveness of RAGT relate to adult stroke: a recently updated Cochrane revision involving 1472 participants showed that RAGT combined with physiotherapy improved recovery of independent walking in patients post stroke. People in the first 3 months after a stroke and those who are not able to walk seem to benefit most from this type of intervention.[15]

The success of studies on adults suggests that RAGT may be well suited to the needs of children, but in the pediatric field evidence is still scarce. Two recent systematic reviews have appraised the evidence for robotic rehabilitation in pediatric gait disorders.[16,17] The reviews reported some positive benefits on activity parameters such as standing ability, walking speed, and distance. However, the studies have highlighted weak and inconsistent scientific evidence regarding the use of robotic rehabilitation in children because of high variation in treatment duration, frequency and outcome measures, and lack of evidence for diagnoses other than CP.

Other studies have also demonstrated positive results after RAGT on locomotion parameters, gait endurance, and functional tasks.[14,18-20] A recent study verified the effect of robotic treatment in a small group of children with CP and demonstrated the usefulness of this robotic gait rehabilitation mainly in the balance control during gait and in the improvement of postural and locomotor functions.[21] Another study demonstrated the effectiveness of RAGT treatment in children with hemiplegia after ABI. The results showed a proximal-to-distal differential effect on the lower limbs and suggested that the participation in RAGT during the acute and/or subacute stage provides positive outcome in terms of global motor abilities, cadence, and gait velocity.[22] However, conflicting results are also reported: Druzbicki et al found no kinematics effect on gait function after robotic gait training in children with CP.[23]

A method to increase the evidence of effectiveness for rehabilitation technologies in children with neurologic impairment is to promote the collaboration between different rehabilitation centers to share common rehabilitation protocols to increase sample sizes and to investigate children with different etiologies and functional abilities.

The Neurorehabilitation Departments of "Bambino Gesù" Children's Hospital and of the Scientific Institute Eugenio Medea started by sharing the experience of physicians, therapists, and engineers to define a common protocol for robotic gait treatment. Both Institutes have been using RAGT devices for many years for the rehabilitation of children with CP or ABI.

In the present retrospective study we examined a large group of children aged 4-18 years with CP and ABI who received a common protocol of evaluation and a combined treatment of RAGT and physical therapy (PT).

The primary aim of the study was to evaluate the effect of RAGT+PT in a large group of children with motor impairment; an additional goal was to compare the effectiveness of the combined RAGT+PT treatment in children with disabilities related to different etiologies (CP and ABI) and with different levels of motor impairment. Finally, we examined the effect of time elapsed from injury (date of brain injury for children with ABI, age for children with CP) on children's functional changes due to RAGT and PT.

List of abbreviations:

ABI	**acquired brain injury**
CP	**cerebral palsy**
GMFCS	**Gross Motor Function Classification System**
GMFM	**Gross Motor Function Measure**
MCID	**minimum clinically important difference**
PT	**physical therapy**
RAGT	**robot-assisted gait training**
6MWT	**6-minute walk test**

Methods

Subjects

In this retrospective study, we included patients who took part in a combined RAGT and PT treatment as inpatients in the Neurorehabilitation Departments of "Bambino Gesù" Children's Hospital in Rome and of the Scientific Institute Eugenio Medea in Bosisio Parini, Italy, between 2012 and 2017.

Inclusion criteria were the diagnosis of ABI or CP, ages 4-18 years, femur length$\geq$23 cm (which corresponds to approximately 4 years of age), and GMFCS levels I-IV. Patients had to be able to report pain, fear, or discomfort reliably and to follow simple instructions. Exclusion criteria were injection of botulinum toxin in lower limbs during the 6 months prior to enrollment, variation in oral skeletal muscle relaxant drug dose in the month prior to treatment, previous orthopedic surgery, severe lower extremity muscle contractures, recent fractures, joint instabilities, osteoporosis, contraindication to full body load for any cause, unhealed skin lesions in the lower extremities, thromboembolic diseases, cardiovascular instability, acute or progressive neurologic disorders, and aggressive or self-harming behavior.

Table 1 Demographic and clinical characteristics of the study sample

Parameter	Entire Sample	ABI	CP	*P* Value
Patients (n)	182	110	72	–
Sex (M/F)	100/82	57/53	43/29	.30
Age at treatment, mean ± SD (y)	10.8±3.8	10.8±4.1	10.8±3.8	.77
Age at injury, mean ± SD (y)	–	9.2±4.3	–	–
Time from injury, mean ± SD (y)	–	1.7±1.9	–	–
Full Scale IQ, mean ± SD	66±19	66±18	67±20	.65
Verbal IQ, mean ± SD	79±19	77±18	81±21	.20
Performance IQ, mean ± SD	66±19	69±18	60±17	.03*

* $P<.05$.

This study was performed in accordance with the Declaration of Helsinki, and approval was obtained (reference GIP-454) by the IRCCS E. Medea Ethics Committee.

The clinical trial has been registered on Clinical Trials.gov: NCT03828110.

Rehabilitation protocol

The rehabilitation protocol consisted of 20 sessions of RAGT and 20 sessions of PT. Every working day (Monday-Friday) and for 4 weeks patients underwent 1 session of RAGT and 1 session of PT, lasting 45 minutes each. Both RAGT and PT were delivered by trained physiotherapists, specialized in the management of pediatric patients. Assessments were performed independently by a different group of physiotherapists blinded to treatment information.

The PT sessions were performed through an intensive program of exercises aimed at strengthening the gluteus and quadriceps muscles, stretching the hip flexor and hamstrings muscles, increasing static and dynamic balance, increasing functional abilities, and improving overground gait and stair climbing.

The RAGT sessions used the Lokomat,[a] an active lower limb exoskeleton with powered hip and knee joints. For all patients, the same group of exercises were offered with initial preset duration, speed, and difficulty. The initial body weight support was set at 50% and was then gradually decreased according to the individual's response to the intervention and to his/her functional capacity. The guidance force was initially set to 100% and then gradually reduced by adjusting the settings. Physiotherapists could vary the guidance force according to the patients' abilities to maximize the intensity of the training and to keep the motivation during each session. A therapist was always present during the child's sessions to follow the progression as well as to raise the child's awareness to correct gait patterns and postures during the training session.

Evaluation

The following demographic and clinical data were collected at baseline: age at treatment, age at injury, time elapsed from injury, sex and etiology (CP or ABI). All patients were classified at admittance according to the Gross Motor Function Classification System (GMFCS).[24] The GMFCS is a 5-level classification system that describes the gross motor function of children and youth on the basis of their self-initiated movement with particular emphasis on sitting, walking, and wheeled mobility.[25] Distinctions between levels are based on functional abilities, the need for assistive technology, including handheld mobility devices or wheeled mobility, and to a much lesser extent, quality of movement.

The cognitive assessment was performed by means of the Wechsler Intelligence Scales, Wechsler Preschool and Primary Scale of Intelligence−Revised and Wechsler Intelligence Scale for Children−Revised, according to chronological age.[26] Before (T0) and at the end of the treatment (T1), all patients underwent a clinical examination that included the Gross Motor Function Measure (GMFM) and the 6-minute walk test (6MWT) only for ambulant patients.

The GMFM measures the child's overall functional abilities and consists of 88 items divided into the following sections: (A) lying and rolling, (B) sitting, (C) crawling and kneeling, (D) standing, and (E) walking, running, and jumping. Each section contributes to the total GMFM score.[27,28]

Table 2 Summary of the linear mixed model for the fixed effects of treatment, etiology, and GMFCS level on 6MWT distance, GMFM total score, and dimensions D and E

		6MWT		GMFM TOT		DIM D		DIM E	
Source of Variation	*df*	F	*P* Value	F	*P* Value	F	*P* Value	F	*P* Value
Within-subject									
Treatment	1	71.99	<.001*	62.60	<.001*	77.58	<.001*	52.47	<.001*
Treatment×GMFCS	2	0.37	.688	0.06	.941	0.32	.725	1.12	.33
Treatment×etiology	1	12.20	.001*	33.19	<.001*	8.81	.003*	28.92	<.001*
Treatment×GMFCS×etiology	2	1.00	.372	0.34	.713	1.66	.193	1.49	.229

Abbreviation: DIM, dimension.
* $P<.05$.

Table 3 Summary of the response variable scores at T0 and T1 for the group as a whole and its stratification according to etiologies and GMFCS

	6MWT		GMFM Total		Dimension D		Dimension E	
Score	T0	T1	T0	T1	T0	T1	T0	T1
ABI								
GMFCS I-II	308±132*	385±112*	202±47*	221±40*	70±23*	81±17*	54±28*	67±22*
GMFCS III	192±115*	265±107*	177±59*	194±53*	62±29*	68±26*	39±26*	48±26*
GMFCS IV	142±151*	188±183*	111±73*	129±78*	27±30*	37±34*	17±24*	25±29*
All GMFCS	233±143*	304±144*	168±69*	187±68*	56±32*	65±31*	39±30*	49±30*
CP								
GMFCS I-II	319±127	342±134	172±71	174±70	73±17	76±14	58±22	59±23
GMFCS III	193±79*	219±89*	150±54	155±54	45±20*	50±20*	27±17	29±19
GMFCS IV	148±73*	179±78*	127±43	129±44	24±16	28±20	15±12	16±13
All GMFCS	222±117*	248±120*	151±59	155±59	48±26*	53±26*	34±25	35±25
Entire sample	228±131*	277±136*	162±66*	174±66*	53±30*	60±30*	37±28*	44±29*

* $P<.05$ between scores at T0 and T1.

The 6MWT was used to assess endurance during self-paced, submaximal walk by measuring the distance walked within 6 minutes along a standardized route through the hospital corridors.[29] A 25-m flat corridor was used, and patients were instructed to walk as far as possible, turning 180° every 25 m. Standardized encouragement was provided to all children by the therapist, regardless of the distance covered. Both institutes used the same protocol of treatment and evaluation.

Statistical analysis

At baseline, differences between patients with CP or ABI were checked using the Mann-Whitney *U* test for continuous variables and the chi-square test for binary variables. A linear mixed model was used to determine the effects of 2 between-subjects fixed factors, that is, GMFCS classification (I-II vs III vs IV) and etiology (ABI vs CP), and 1 within-subjects fixed effect, that is, treatment (T0 vs T1), on each response variable with patients as a random factor. The response variables included 6MWT distance, GMFM total score, and GMFM dimensions D and E. Significant differences in each response variable between the etiologies within each GMFCS level as well as differences across GMFCS levels were compared by post hoc tests adjusted by the least significant difference adjustment to identify pairwise differences ($P<.05$). To explore the influence of the time elapsed from injury as a covariate on the response variables, the linear mixed model was adjusted for this variable ($P<.05$).

Results

Data from 182 children with GMFCS levels I-IV were included in the study, 110 with ABI and 72 with CP. Table 1 reports the demographic and clinical data for the entire sample and for the children with ABI and CP. A total of 152 participants completed the 6MWT both at T0 and T1. The cognitive assessment was carried out at the beginning of the treatment. At admission in the rehabilitation hospital, the only statistically significantly different parameter between children with ABI and CP at T0 was Performance IQ, which was higher in patients with ABI than children with CP (69 and 60, respectively). No significant correlations between changes in clinical scales and the values of cognitive assessment were found.

Table 4 Summary of the differences between T0 and T1 for all response variable scores for the group as a whole and its stratification according to etiologies and GMFCS, with associated *P* values

	6MWT		GMFM Total		Dimension D		Dimension E	
Score (%)	T1-T0	*P* Value	T1-T0	*P* Value	T1-T0	*P* Value	T1-T0	*P* Value
ABI								
GMFCS I-II	+50 (16)	<.001*	+19 (7.2)	<.001*	11	<.001*	13	<.001*
GMFCS III	+68 (35)	<.001*	+17 (6.4)	<.001*	7	<.001*	9	<.001*
GMFCS IV	+37 (26)	.010*	+18 (6.8)	<.001*	10	<.001*	7	<.001*
All GMFCS	+57 (25)	<.001*	+18 (6.8)	<.001*	9	<.001*	10	<.001*
CP								
GMFCS I-II	+23 (7)	.075	+2 (0.8)	.634	6	.075	1	.617
GMFCS III	+25 (13)	.023*	+5 (1.9)	.122	4	.002*	2	.189
GMFCS IV	+31 (21)	.034*	+3 (1.1)	.615	4	.072	1	.699
All GMFCS	+26 (12)	.001*	+3 (1.1)	.172	5	.001*	2	.234
Entire sample	+49 (19)	<.001*	+14 (5.3)	<.001*	7	<.001*	7	<.001*

* $P<.05$ between scores at T0 and T1.

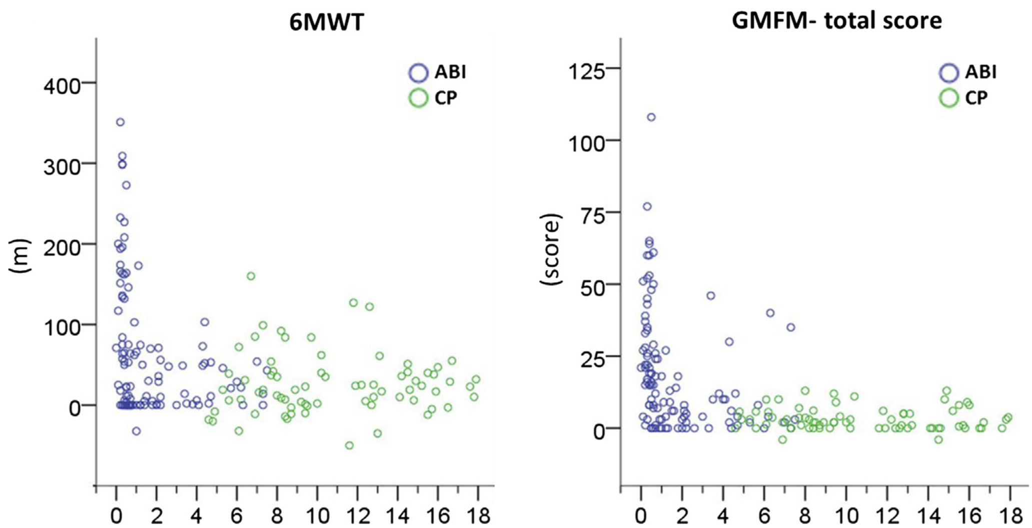

Fig 1 Relationship between change scores of the 6MWT and the GMFM total score and time from injury for patients with ABI (blue circles) and patients with CP (green circles).

According to the GMFCS levels, in the group of children with ABI, 42 patients were assigned to class I-II, 38 were assigned to class III, and 30 were assigned to class IV. In the group of children with CP, 23 patients were assigned to class I-II, 31 were assigned to class III, and 18 were assigned to class IV.

The statistical analysis showed highly significant effects for treatment and the interaction between treatment and etiology for all the response variables (table 2). Summary of the scores at T0 and T1 for the group as a whole and its stratification according to etiologies and GMFCS is shown in table 3. Differences between scores at T0 and T1 with *P* values of the post hoc tests are shown in table 4.

Figure 1 shows the relationship between change scores of the 6MWT and the GMFM total score and time from injury. The results of the linear mixed model adjusted for the variable time elapsed from injury showed that, after controlling for the covariate, no significant interaction between treatment and etiology was found for any of the response variables (6MWT: $F=0.37$, $P=.544$; GMFM total score: $F=2.25$, $P=.136$; dimension D: $F=0.01$, $P=.947$; dimension E: $F=0.91$, $P=.342$) (table 5).

Discussion

The scientific evidence regarding the use of robotic rehabilitation in children is still weak and inconsistent.[16,17] To overcome some of the existing limitations, we aimed to evaluate the effectiveness of a combined RAGT and PT treatment in 182 children with neurologic impairment, comparing the effectiveness of the combined RAGT+PT treatment in children with different etiologies (ABI and CP) and with different levels of function (according to GMFCS). Finally, we examined the effect of time after injury on the functional changes.

A significant improvement emerged in the 6MWT in the whole group and in the 2 subgroups (ABI and CP), confirming recent studies: Meyer-Heim et al reported comparable mean improvements in distance walked (+13%) in a group of 67 children with CP treated with the same protocol,[20] while Beretta et al showed improvements of +19% in a group of 29 children with ABI.[22] Estimates of the minimum clinically important difference (MCID) in pediatric populations after RAGT treatment are still lacking for clinical tests evaluating walking endurance, such as the 6MWT.[30] However, relative mean improvements of 25% and 12% for populations with ABI and CP obtained in our study are

Table 5 Summary of the linear mixed model for the effects of treatment, etiology and GMFCS level on 6MWT distance, GMFM total score, and dimensions D and E, controlling for the variable time elapsed from injury

		6MWT		GMFM Total		DIM D		DIM E	
Source of Variation	df	F	*P* Value	F	*P* Value	F	*P* Value	F	*P* Value
Within-subject									
Treatment	1	29.56	<.001*	34.03	<.001*	32.73	<.001*	28.72	<.001*
Treatment×time elapsed from injury	1	3.45	.065	5.5	.02*	4.39	.038*	5.94	.016*
Treatment×GMFCS	2	0.31	.732	0.11	.896	0.33	.718	1.49	.228
Treatment×etiology	1	0.37	.544	2.25	.136	0.01	.947	0.91	.342
Treatment×GMFCS×etiology	2	0.524	.593	0.59	.555	2.05	.131	1.54	.217

Abbreviation: DIM, dimension.
* $P<.05$.

generally within or above the range of MCID identified by a recent systematic review in patients with respiratory, cardiovascular, and muscular diseases.[31] Progress was also obtained in global improvement of gross motor capacity. The GMFM total score improved significantly in the whole group and in the patients with ABI but not in the group of patients with CP, confirming previous research.[32] This is also observable in GMFM dimensions D and E, which highlighted global enhancement in patients' standing and walking abilities but less improvements in patients with CP compared with ABI.[20] Our study agrees with previous research demonstrating the effectiveness of RAGT treatment in gross motor abilities of children with CP, with mean variations in both GMFM dimensions D and E that are comparable with existing literature.[33] Our results also showed higher improvements in dimension D than dimension E in patients with CP, a finding that is supported by previous literature.[14] Our study reports improvements that are above MCID thresholds identified by Oeffinger et al in a population of ambulatory children with CP.[34] Unfortunately, no MCID estimates have been published yet for children with ABI.

We also analyzed the response to treatment of children according to the GMFCS, as suggested by a recent consensus guideline,[35] highlighting the need for studies aimed at clarifying how variables such as severity of impairment and age of the patients may influence the effectiveness of these therapies. Previous research focusing on improvements in populations with CP stratified according to GMFCS levels has been contradictory so far, with a study showing greater improvements in mildly affected patients (GMFCS I and II),[36] while others highlighted that more severely affected children may benefit more of RAGT training.[37] Our results showed that, after RAGT and PT treatment, children affected by ABI obtained significant improvements in all GMFCS levels, whereas in children with CP, only patients at GMFCS level III seem to benefit from robotic rehabilitation. This evidence suggests that in patients with CP, the best results are obtained in patients who walk using a handheld mobility devices or may climb stairs holding onto a railing with supervision or assistance. We hypothesize a ceiling effect in patients with CP and functional levels GMFCS I and II who have not obtained significant improvements from treatment, having already achieved good walking performance.

Our study also highlights the role of time elapsed from injury as a covariate explaining the different improvements between patients with ABI and CP. In fact, in our study, patients with ABI are treated soon after the acute event compared with the group of patients with CP who access the treatment later (mean age at treatment for patients with CP, 10.8±3.8) when the gait pattern is stabilized.[25] This result suggests that response differences between etiologies may be essentially because of the time elapsed from injury, indicating that the sooner the combined treatment is carried out, the greater the chances are that it will be effective.

Study limitations

The main study limitation is the lack of a comparison group performing a different rehabilitative treatment that may support the critical evaluation of the RAGT efficacy. As a consequence, reported changes in outcome measures are the result of the contribution of both RAGT+PT treatment and of the natural history of CP or ABI. Moreover, in this study only pre- and post-treatment evaluations were presented and no follow-up period was included, and the outcome measures were limited to 6MWT and GMFM score, with no measure of functional and/or independence aspects of daily life. In addition, quantitative measures such as gait analysis may provide further insights in the treated cohort. Lastly, although GMFCS has been already used for the description of patients with ABI,[24] we are not aware of any thorough validation in children with this pathology.

Conclusions

The present study investigated the effectiveness of a combined RAGT+PT treatment in a large group of children with central gait impairment. We demonstrated the positive results for the whole group and the substantial differences between CP and ABI subgroups with better results for children with ABI, which seems to be consistently because of to the shorter time elapsed from injury. Our study has interesting clinical implications: it highlights differences in treatment response between children with different etiologies and functionalities, suggesting the need to adapt the goal of the rehabilitation according to these features. Furthermore, the study highlights the importance of proposing robot-assisted treatment as early as possible during the developmental age, when the gait pattern and the evolution of the motor abilities are still modifiable.

Supplier

a. Lokomat; Hocoma AG.

Keywords

Brain injuries; Cerebral palsy; Neurological rehabilitation; Rehabilitation

Corresponding author

Elena Beretta, MD, Scientific Institute, IRCCS "E. Medea," Acquired Brain Injury Unit, Bosisio Parini, Lecco, Italy. *E-mail address:* elena.beretta@lanostrafamiglia.it.

References

1. Rosenbaum P, Paneth N, Leviton A, et al. A report: the definition and classification of cerebral palsy April 2006. Dev Med Child Neurol 2007;109:8-14.
2. Surman G, Hemming K, Platt MJ, et al. Children with cerebral palsy: severity and trends over time. Paediatr Perinat Epidemiol 2009;23:513-21.
3. Wong CP, Forsyth RJ, Kelly TP, Eyre JA. Incidence, aetiology, and outcome of non-traumatic coma: a population based study. Arch Dis Child 2001;84:193-9.
4. Gazzellini S, Strazzer S, Stortini M, et al. Pediatric rehabilitation of severe acquired brain injury: a multicenter survey. Eur J Phys Rehabil Med 2012;48:423-31.
5. Catroppa C, Rosenfeld JV, Anderson VA, Hearps SS, Godfrey C. Functional recovery ten years after pediatric traumatic brain injury: outcomes and predictors. J Neurotrauma 2012;29:2539-47.
6. Novak I, Mcintyre S, Morgan C, et al. A systematic review of interventions for children with cerebral palsy: state of the evidence. Dev Med Child Neurol 2013;55:885-910.

7. Baque E, Sakzewski L, Barber L, Boyd RN. Systematic review of physiotherapy interventions to improve gross motor capacity and performance in children and adolescents with an acquired brain injury. Brain Inj 2016;30:948-59.
8. Castelli E. Robotic movement therapy in cerebral palsy. Dev Med Child Neurol 2011;53:481.
9. Winchester P, McColl R, Querry R, et al. Changes in supraspinal activation patterns following robotic locomotor therapy in motor-incomplete spinal cord injury. Neurorehabil Neural Repair 2005;19: 313-24.
10. Luft AR, MacKo RF, Forrester LW, et al. Treadmill exercise activates subcortical neural networks and improves walking after stroke: a randomized controlled trial. Stroke 2008;39:3341-50.
11. Labruyère R, Gerber CN, Birrer-Brütsch K, Meyer-Heim A, van Hedel HJ. Requirements for and impact of a serious game for neuro-pediatric robot-assisted gait training. Res Dev Disabil 2013; 34:3906-15.
12. Koenig A, Wellner M, Koneke S, Meyer-Heim A, Lunenburger L. Virtual gait training for children with cerebral palsy using the Lokomat gait orthosis. Stud Health Technol Inform 2008;132:204-9.
13. Aurich-Schuler T, Grob F, Van Hedel HJ, Labruyère R. Can Lokomat therapy with children and adolescents be improved? An adaptive clinical pilot trial comparing Guidance Force, Path Control, and FreeD. J Neuroeng Rehabil 2017;14:76.
14. Schroeder AS, Homburg M, Warken B, et al. Prospective controlled cohort study to evaluate changes of function, activity and participation in patients with bilateral spastic cerebral palsy after robot-enhanced repetitive treadmill therapy. Eur J Paediatr Neurol 2014;18:502-10.
15. Mehrholz J, Thomas S, Werner C, Kugler J, Pohl M, Elsner B. Electromechanical-assisted training for walking after stroke. Cochrane Database Syst Rev 2017;5:CD006185.
16. Lefmann S, Russo R, Hillier S. The effectiveness of robotic-assisted gait training for paediatric gait disorders: systematic review. J Neuroeng Rehabil 2017;14:1.
17. Carvalho I, Pinto SM, Chagas Ddas V, Praxedes dos Santos JL, de Sousa Oliveira T, Batista LA. Robotic gait training for individuals with cerebral palsy: a systematic review and meta-analysis. Arch Phys Med Rehabil 2017;98:2332-44.
18. Wallard L, Dietrich G, Kerlirzin Y, Bredin J. Robotic-assisted gait training improves walking abilities in diplegic children with cerebral palsy. Eur J Paediatr Neurol 2017;21:557-64.
19. Borggraefe I, Meyer-Heim A, Kumar A, Schaefer JS, Berweck S, Heinen F. Improved gait parameters after robotic-assisted locomotor treadmill therapy in a 6-year-old child with cerebral palsy. Mov Disord 2008;23:280-3.
20. Meyer-Heim A, Ammann-Reiffer C, Schmartz A, et al. Improvement of walking abilities after robotic-assisted locomotion training in children with cerebral palsy. Arch Dis Child 2009;94:615-20.
21. Wallard L, Dietrich G, Kerlirzin Y, Bredin J. Effect of robotic-assisted gait rehabilitation on dynamic equilibrium control in the gait of children with cerebral palsy. Gait Posture 2018;60:55-60.
22. Beretta E, Molteni E, Biffi E, Morganti R, Avantaggiato P, Strazzer S. Robotically-driven orthoses exert proximal-to-distal differential recovery on the lower limbs in children with hemiplegia, early after acquired brain injury. Eur J Paediatr Neurol 2018;22:1-10.
23. Druzbicki M, Rusek W, Snela S, et al. Functional effects of robotic-assisted locomotor treadmill therapy in children with cerebral palsy. J Rehabil Med 2013;45:358-63.
24. Jackman M, Novak I, Lannin N. Effectiveness of functional hand splinting and the cognitive orientation to occupational performance (CO-OP) approach in children with cerebral palsy and brain injury: two randomised controlled trial protocols. BMC Neurol 2014;14:144.
25. Palisano R, Rosenbaum P, Walter S, Russell D, Wood E, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol 1997; 39:214-23.
26. Wechsler D. WAIS-R Manual: Wechsler Adult Intelligence Scale - Revised; 1981.
27. Russell DJ, Rosenbaum PL, Cadman DT, Gowland C, Hardy S, Jarvis S. The Gross Motor Function Measure: a means to evaluate the effects of physical therapy. Dev Med Child Neurol 1989;31:341-52.
28. Linder-Lucht M, Othmer V, Walther M, et al. Validation of the gross motor function measure for use in children and adolescents with traumatic brain injuries. Pediatrics 2007;120:e880-6.
29. Andersson C, Asztalos L, Mattsson E. Six-minute walk test in adults with cerebral palsy. A study of reliability. Clin Rehabil 2006;20:488-95.
30. Booth AT, Buizer AI, Meyns P, Oude Lansink IL, Steenbrink F, van der Krogt MM. The efficacy of functional gait training in children and young adults with cerebral palsy: a systematic review and meta-analysis. Dev Med Child Neurol 2018;60:866-83.
31. Schrover R, Evans K, Giugliani R, Noble I, Bhattacharya K. Minimal clinically important difference for the 6-min walk test: literature review and application to Morquio A syndrome. Orphanet J Rare Dis 2017;12:78.
32. Meyer-Heim A, Borggraefe I, Ammann-Reiffer C, et al. Feasibility of robotic-assisted locomotor training in children with central gait impairment. Dev Med Child Neurol 2007;49:900-6.
33. Borggraefe I, Kiwull L, Schaefer JS, et al. Sustainability of motor performance after robotic-assisted treadmill therapy in children: an open, non-randomized baseline-treatment study. Eur J Phys Rehabil Med 2010;46:125-31.
34. Oeffinger D, Bagley A, Rogers S, et al. Outcome tools used for ambulatory children with cerebral palsy: responsiveness and minimum clinically important differences. Dev Med Child Neurol 2008;50:918-25.
35. Aurich-Schuler T, Warken B, Graser JV, et al. Practical recommendations for robot-assisted treadmill therapy (Lokomat) in children with cerebral palsy: indications, goal setting, and clinical implementation within the WHO-ICF framework. Neuropediatrics 2015;46:248-60.
36. Borggraefe I, Schaefer JS, Klaiber M, et al. Robotic-assisted treadmill therapy improves walking and standing performance in children and adolescents with cerebral palsy. Eur J Paediatr Neurol 2010;14: 496-502.
37. van Hedel HJ, Meyer-Heim A, Rüsch-Bohtz C. Robot-assisted gait training might be beneficial for more severely affected children with cerebral palsy. Dev Neurorehabil 2016;19:410-5.