Annals of Biomedical Engineering (© 2018)
https://doi.org/10.1007/s10439-018-2039-1

Immersive Virtual Reality to Improve Walking Abilities in Cerebral Palsy: A Pilot Study

Chiara Gagliardi, Anna Carla Turconi, Emilia Biffi, Cristina Maghini, Alessia Marelli, Ambra Cesareo, Eleonora Diella, and Daniele Panzeri

Scientific Institute, IRCCS Eugenio Medea, Bosisio Parini, Lecco, Italy

(Received 14 December 2017; accepted 24 April 2018)

Associate Editor Kerry Hourigan oversaw the review of this article.

Abstract—Immersive virtual reality (IVR) offers new possibilities to perform treatments in an ecological and interactive environment with multimodal online feedbacks. Sixteen school-aged children (mean age 11 ± 2.4 years) with Bilateral CP—diplegia, attending mainstream schools were recruited for a pilot study in a pre–post treatment experimental design. The intervention was focused on walking competences and endurance and performed by the Gait Real-time Analysis Interactive Lab (GRAIL), an innovative treadmill platform based on IVR. The participants underwent eighteen therapy sessions in 4 weeks. Functional evaluations, instrumental measures including GAIT analysis and parental questionnaire were utilized to assess the treatment effects. Walking pattern (stride length left and right side, respectively $p = 0.001$ and 0.003; walking speed $p = 0.001$), endurance (6MWT, $p = 0.026$), gross motor abilities (GMFM-88, $p = 0.041$) and most kinematic and kinetic parameters significantly improved after the intervention. The changes were mainly predicted by age and cognitive abilities. The effect could have been due to the possibility of IVR to foster integration of motor/perceptual competences beyond the training of the walking ability, giving a chance of improvement also to older and already treated children.

Keywords—Immersive virtual reality, Gait rehabilitation, Children, Cerebral palsy.

INTRODUCTION

Cerebral palsy (CP) is a neurodevelopmental disorder characterized by movement and posture disorders causing activity limitation.[2] It is the most severe physical disability within the spectrum of developmental delay, beginning in early childhood and persisting through the lifespan, and accompanied by a spectrum of comorbidities unevenly distributed and affecting also the neurocognitive profile (including sensation, cognition, communication, perception and behavior). Currently, the standard of care for the motor disorder in CP consists of physical therapy offered mainly in early childhood through preadolescence together with a spectrum of concurrent medical and surgical interventions. The intervention aims at improving activity and participation thanks to the maintenance of the status quo or to the minimization of future deformity or disability.[9] When suitable, walking ability and efficient gait are among the primary therapeutic goals for children with CP, given also the role of predictor of reduced capacity for activity, participation, and social interaction for which the decreased locomotor functions are accredited.[28]

The large focus of motor rehabilitation is on developing motor skills to improve the child's performance in meaningful activities. Traditional approaches promote repetition as the main way, but the lack of motivation due to repetition is the frequent basis of drop outs and lack of efficacy of the intervention. Context and engagement are fundamental, but it is often difficult to create a motivating and ecological context in traditional rehabilitation settings. Real-life settings are a possibility to offer meaningful activities, but often with a "global" and not precise feedback of the performance, not to mention the difficulty to create the real life conditions tailored to each patient. Both intrinsic (individual perception) and extrinsic (effect of the action) feedbacks are fundamental to the modification of the motor performance.

Among more traditional physiotherapy treatments, the treadmill training has proved effective in facilitat-

---

Address correspondence to Chiara Gagliardi, Scientific Institute, IRCCS Eugenio Medea, Bosisio Parini, Lecco, Italy. Electronic mails: chiara.gagliardi@bp.lnf.it, annacarla.turconi@lanostrafamiglia.it, emilia.biffi@bp.lnf.it, cristina.maghini@bp.lnf.it, giocacusano@tiscali.it, ambra.cesareo@bp.lnf.it, eleonora.diella@bp.lnf.it, daniele.panzeri@bp.lnf.it

ing the attainment of locomotion and walking, as well as of a gait pattern more similar to normal.[23] Treadmill training is indeed an approach based on an active, repetitive, task-specific approach according to current theories of motor learning. Also technological devices such as robotic orthoses has been recently proposed for gait recovery in children with neurological pathologies.[12,22,29]

Recently the standard treatments have been supported by modern technologies that use Virtual reality and real-time feedback. Satisfactory results have been achieved in motor and cognitive rehabilitation of adults[7,16,26] and CP children[20,30] by means of VR systems. Cho and collaborators showed that the improvements of walking abilities with VR were even bigger than those obtained in a traditional treadmill training group (without VR).[8] Unfortunately, no evaluations concerning the gait pattern and the kinetic/kinematic parameters while walking were performed in that study.

The further technological step has been the possibility to utilize immersive virtual reality environments (IVR), which help in increasing the patient's motivation thanks to a more ecological and interactive experience coupled with an enriched environment and multimodal feedback. The Gait Real-time Analysis Interactive Lab (GRAIL) by Motek Medical (the Netherlands) is a platform based on an instrumented dual-belt treadmill, a two degrees of freedom motion frame and an immersive VR system. Nowadays it is recognized by the community as a platform for the evaluation and rehabilitation of adults affected by neurologic and orthopedic pathologies.[3,10,13,17–19,21,31] Further, this system has been used to evaluate the gait pattern in children with typical development and with cerebral palsy.[33,38,39] In 2017, Van Gelder *et al.* demonstrated in a group of ambulatory children with CP significant and clinically relevant improvements in peak hip and knee extension after a focused treatment performed on Grail platform with specific real time feedback of the performance.[40] They suggested as key finding that the gait remains adaptable in children with CP, despite the motor control and gait kinematic/kinetic parameters are often thought to be relatively rigid in this population.

The aim of this pilot study was to verify the efficacy in terms of walking abilities and gait pattern of an intensive rehabilitative treatment on a GRAIL system in a group of ambulatory children affected by bilateral CP. We proposed an ecological situation, where the modifications were to be implemented by the participant on the basis of an increased efficacy of his/her performance, as by the feedback provided by the virtual environment. We hypothesized that walking abilities as a whole could be positively affected by the intervention and at least partially modifiable even beyond early childhood.

MATERIALS AND METHODS

Participants

Patients were recruited at the Scientific Institute E. Medea, Bosisio Parini, Italy. The inclusion criteria were as follows: diagnosis of bilateral CP; age between 7 and 16 years old; able to walk independently with no or minimal assistance or with hand-held mobility device (severity of motor impairment classified in level I, II and III, according to gross motor function classification system (GMFCS)[27]); sufficient cognitive ability to follow the instructions. The exclusion criteria were as follows: severe muscle spasticity and/or contracture (Ashworth Scale Score ≥ 3),[5] a diagnosis of severe learning disability, behavioral problems, and visual or hearing difficulties that would impact on the proposed activity and participation. Children were excluded if they had received botulinum toxin-A treatment within 16 weeks prior to measurement date; or orthopaedic surgery, intrathecal baclofen treatment or selective dorsal rhizotomy in the previous 12 months.

According to these criteria, 16 children with bilateral CP were recruited: 10 males, 6 females; mean age 11 ± 2.4 years old and GMFCS I/II/III: 7/7/2 (Table 1 for details).

General intelligence was assessed by age-appropriate Wechsler Intelligence Scales.[41] No particular adaptation of standard test conditions was necessary, apart from postural adaptations and handling facilities.

As reference data, we used gait information acquired on 10 young healthy adults (HA), who were previously enrolled in a study on GRAIL (mean age 26 ± 1.7 years old, 1 male, 9 females; see Ref. 4).

TABLE 1. Participants' details at baseline.

	Patients
Sample size	16
Gender (M/F)	10/6
Age* (years)	11 ± 2.4
GMFCS (I/II/III)	7/7/2
Ashworth Scale Score (1/2)	7/9
Full IQ**	70 (22)
Verbal IQ**	78 (26)
Performance IQ**	64 (31)
Verbal comprehension**	84.5 (22)
Perceptive organization**	71 (29.3)

*Mean ± standard deviation.
**Median (IQR).

The study protocol was approved by the Ethics Committee of Scientific Institute E. Medea. Written consent was obtained from the parents of each patient.

The GRAIL System

The GRAIL system (Fig. 1) is a platform which integrates a treadmill on a motion frame, a Vicon motion-capture system (Oxford Metrics, Oxford, UK) and a 180° cylindrical projection screen (see Ref. 4 for a thorough description of the system). The whole system is controlled by the D-flow, a software that oversees the relationship between the subject, the scenario and the interactive feedbacks and stimulations. The D-flow runs on Microsoft Windows and it is designed for the development of interactive and immersive virtual reality applications where the subject is a central part of a real-time feedback loop. The system operator defines feedback strategies through a flexible and extensible application development framework, based on visual programming. The D-flow programming, indeed, is based on the concept of modules, that are components with a specific functionality, which can be combined to create complex, interactive virtual reality applications. Some modules directly control specific hardware devices, such as a treadmill or a motion base. Other modules provide access to real-time data streams from live input devices. Others manipulate virtual objects or detect collisions between them, thus allowing the interaction between the subject and the virtual environment. In addition to data-based communication, the D-flow kernel framework allows event-based communication between modules.[15]

Rehabilitation Treatment

All CP children underwent a 4-week training, with one daily session lasting 30 min, 5 days a week, for a total of 18 rehabilitative sessions on GRAIL in the period plus two evaluation sessions on GRAIL at the beginning and end of the period. The treatment included exercises to improve walking and balance abilities using engaging VR environments (e.g. transfer your load from the left to the right side to avoid obstacles while skiing; shoot balls at targets inside a goal; walk in a forest as fast as possible; hit as many elves as possible by squatting, and so on). Participants performed exercises belonging to six groups, accordingly to their rehabilitative goals and aimed at increasing:

- the efficiency in load transfer;
- the ability to maintain monopodalic load;
- their walking activity and endurance;
- the ability of dynamic balance;
- the width of joints range of motion;
- their overall motor coordination.

The participants were allowed to use their shoes/AFOs as they were used to in daily living. No mobility device was needed during the training on the GRAIL system.

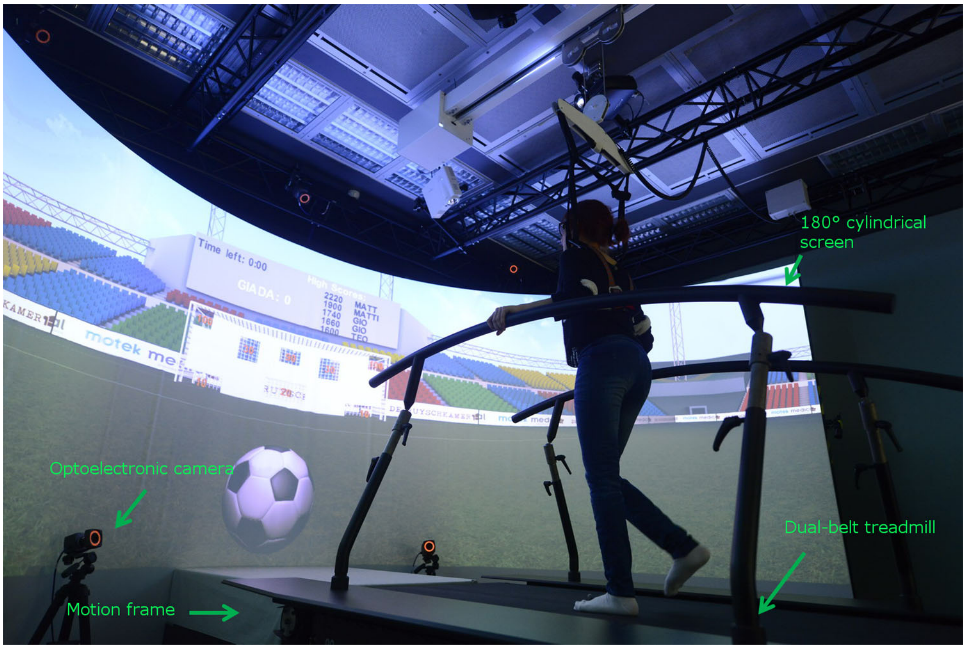

FIGURE 1. The GRAIL system (color).

The treatment was conducted by experienced physiotherapists after a training certified by Motekforce Link trainers.

During the pilot study other interventions—if any—were suspended.

Assessment Measures

The treatment aimed at improving mobility, endurance, balance and overall coordination and fluency (timing and speediness). In order to verify the pre/post treatment variations, three groups of measures were selected as outcome indexes:

1. Functional evaluations by means of standardized scales administered the day before the beginning (T0) and the day after the end of the intervention (T1) by a team of physiotherapists, different from those who administered the treatment on the GRAIL.

   Overall motor functional abilities were assessed by the Gross Motor Function Measure (GMFM) which consists of 88 items, divided into 5 sections: (A) lying and rolling; (B) sitting; (C) crawling and kneeling; (D) standing; (E) walking, running and jumping. Each section contributes to the total GMFM score (range 0–100). The improvement of the GMFM 88 score was set as main outcome index, with 2 as minimum clinically important differences (MCID).[25]

   The gait endurance was assessed *via* the Six-Minute Walking Test (6MWT), a self-paced, submaximal test of the capability of walking. The child had to walk over ground and to cover as much distance as possible in 6 min along a standardized route.[1]
2. Instrumental measures were performed at T0 and T1 as follows.

   Energy expenditure during 6MWT was measured by means of the wearable device Sensewear Armband (BodyMedia, Inc., Pittsburgh, PA), which utilizes a 3 axis accelerometer, heat flux sensor, galvanic skin response sensor (GSR), skin temperature sensor, and a near body ambient temperature sensor to capture data leading to the calculation of energy expenditure. Patients were asked to wear the Armband on the back of the left upper arm during the 6MWT.

   Gait analysis was performed on the GRAIL; the children were asked to walk barefoot or to wear their usual orthoses or footwear. The procedure required a 6-min adaptation period, then subjects were asked to walk at a self-elected fixed speed with no feedback on the GRAIL treadmill for 3 min and at least 20 steps were acquired for each minute (as in Ref.4). As reference data, we used gait data collected on healthy adults who walked at fixed-speed and in self-paced configuration for 10 min/each setting, after a 6-min familiarization period. Consecutive measurements were performed and the mean values of kinematic parameters were computed on 274 ± 85 steps. Kinematics and kinetics were computed by means of the 25-marker Human Body Model.[37] Specifically, the following parameters were calculated: the percentage of stance with respect to the whole step cycle (stance time, %), the step width, the stride length, the stride time, the walking speed, the peak of power during ankle flex-extension (max ankle FE power), the maximum extension of ankle in swing (min ankle FE swing), the ankle range of motion during stance (ROM of ankle FE stance) and swing (ROM of ankle FE swing), the knee flexion at initial contact, the maximum extension of knee (min FE of knee), the knee range of motion during flexo-extension (ROM of knee FE), the maximum hip extension (min FE of hip), the hip range of motion during flexo-extension (ROM of hip FE) and abdo-adduction (ROM of hip ABAD), the range of motion of pelvic tilt and of pelvic obliquity.
3. Parent completed questionnaire referred to everyday life before and after the intervention.

   The spillover of the treatment on walking in ecological environment was assessed by the 10-level classification of ambulatory function in everyday-life provided by the Functional Assessment Questionnaire (FAQ). The relatives or caregivers were asked to score the walking ability of their children.[24] The same proxy answered to the questionnaire twice (pre and post treatment).

The improvement of the GMFM 88 score was set as main outcome index. As to sample size, we considered 2 as a minimum significant change of GMFM 88 (main outcome index), 3.5 the among subjects standard deviation, 0.8 the correlation between pre/post treatment measures and 5 and 10 as respectively alpha and beta errors. The required sample size was 16 participants.

Data Analysis

The overall energy expenditure (EE) estimated by the Armband was used to compute

- the energy expenditure per minute (EEMin) [kJ min^{-1}], an index of metabolic consumption for each minute walked,

- the energy expenditure per meters (EEM) [kJ m^{-1}], an index of metabolic consumption for each meter walked.

Data acquired during gait analysis were analyzed as follows. Real-time filtering of the markers' traces was performed with a 2nd order Butterworth filter, with a cutoff frequency of 6 Hz. Valid gait cycles were recognized automatically by the Gait Offline Analysis Tool, then gait traces, forces, moments and powers of valid cycles were saved in a csv file. Spatiotemporal parameters, such as walking speed, stance duration, stride length and step width, and kinematic and kinetic parameters of pelvis, hip, knee and ankle were computed as previously done.[4,34,39] The mean and standard deviation of these parameters were calculated across the collected steps. Given the frequently prevailing involvement of one side, we analyzed separately the data related to each side.

Statistical Analysis

The non-normality of the group of patients was evaluated by the Shapiro–Wilk test. Therefore, data are presented as median and interquartile range (IQR, computed as the 75th percentile minus the 25th percentile) and the paired non-parametric Wilcoxon test was performed to compare functional evaluations, instrumental measures and the questionnaire results of patients before and after the rehabilitation treatment.

The Mann–Whitney test was used to evaluate changes of patients' gait data with respect to healthy adult (HA).

A linear regression analysis was performed on the change of functional evaluations and questionnaire to model the relationship between variables and to verify if there is a model (or more) that could predict the results obtained. In particular, age, performance and verbal IQ (pIQ and vIQ), and GMFCS and their combination were tested as regressors.

The significance level was set at $p < 0.05$.

RESULTS

All the patients completed the whole rehabilitative program; only 1 patient performed 17 sessions.

IQ scores are shown in Table 1.

Functional and instrumental results pre—post intervention are detailed in Tables 2 and 3, respectively.

Gross motor competences improved after treatment (Table 2), mainly in the D (capacity of standing) and E (capacity of walking, running and jumping) dimensions of GMFM scale (pre–post treatment changes of: GMFM-88 $p = 0.041$; GMFM D $p = 0.041$; GMFM E $p = 0.017$). The endurance improved significantly as by the increase of distance walked in the 6MWT ($p = 0.026$).

TABLE 2. Results about the functional scales at T0 and T1.

	Median (IQR) T0	Median (IQR) T1	*p* values
GMFM-88	81 (19.5)	81.5 (18.5)	**0.041**
GMFM-A	100 (4)	100 (4)	1
GMFM-B	100 (3)	100 (2.25)	0.317
GMFM-C	95 (24.5)	95 (24.5)	0.180
GMFM-D	79 (20.5)	79 (18.75)	**0.041**
GMFM-E	52.5 (54)	55 (53.75)	**0.017**
6-MWT (m)	373.2 (176.8)	385 (156.125)	**0.026**
FAQ	8 (0.25)	8 (1)	0.083

Values expressed as median (interquartile range). Bold values mean $p < 0.05$.

The energy expenditure per minute (EEMin T0: 18.08 (12.68), T1: 19.08 (8.33)) as well as the EE per meter walked (EEM T0: 0.33 (0.21), T1: 0.32 (0.18)) did not show any significant changes due to the intervention.

The kinematic and kinetic data were computed in average over 25 (11.3) valid cycles at T0 and T1.

Table 3 reports patients' scores before (P T0) and after (P T1) the rehabilitation treatment. The patients' performance is compared to HA and to data obtained in typically developing children (TD, 4 females; 10.6 ± 2.2 (8–15) years old) reported in previous studies.[33,38,39]

We observed a significant bilateral improvement of the stride length ($p = 0.001$ L, 0.003 R) and of the walking speed ($p = 0.001$ L, 0.002 R) as well as a reduction of the step width and of the stance time. Further, we observed a significant increase of the peak of power at the ankle level ($p = 0.004$ L) as well as an improvement of the range of motion (ROM) of the ankle flexo-extension (FE) in stance ($p = 0.022$ L, 0.048 R) and swing ($p = 0.002$ L, 0.008 R). Moreover, data evidenced the reduction of the excessive knee flexion at initial contact ($p = 0.011$) and the enhancement of the ROM in FE ($p = 0.023$ L, 0.001 R) and adb-adduction ($p = 0.023$ R) at the hip level. Finally, improvements in terms of tilt ($p = 0.041$ L, 0.005 R) and obliquity ($p = 0.008$ L, 0.009 R) ROM were measured at the pelvis. Changes in patients' walking pattern tended towards the pattern both of HA and TD except for the ROM of pelvic tilt.

No significant change pre–post treatment was detected *via* the FAQ.

Concerning the regression analysis, gross motor level of impairment (GMFCS), cognitive competences (as by verbal and performance IQ) and chronological age were predictor factors for the pre–post treatment

TABLE 3. P refers to patients, HA to healthy adults, TD to typically developing children as described in Refs. 33,38,39

Gait parameter	side	P T0Median (IQR)	P T1Median (IQR)	HAMedian (IQR)	TDMean (std)
Stance time (%)	L	74.40 (6.24)*	72.09 (5.92)*	66.49 (1.99)	64.77 ± 1.47
	R	72.68 (6.1)*	71.86 (7.61)*		
Step width (m)	L	0.13 (0.08)*	0.11 (0.07)*	0.08 (0.03)	0.12 ± 0.01
	R	0.13 (0.07)*	0.13 (0.08)*		
Stride length (m)	L	0.82 (0.14)*	**1.03 (0.13)***	1.22 (0.19)	1.28 ± 0.03
	R	0.82 (0.12)*	**1.05 (0.28)***		
Stride time (s)	L	1.50 (0.39)*	1.52 (0.45)*	1.10 (0.12)	1.07 ± 0.03
	R	1.50 (0.37)*	1.38 (0.43)*		
Walking speed (m/s)	L	0.51 (0.23)*	**0.72 (0.18)***	1.10 (0.37)	1.29 ± 0.06
	R	0.53 (0.26)*	**0.65 (0.22)***		
Max ankle FE power (W/kg)	L	0.59 (0.37)*	**1.04 (0.43)***	2.69 (0.97)	1.47 ± 0.12
	R	0.83 (0.37)*	0.85 (0.60)*		
Min ankle FE swing (°)	L	1.23 (7.46)*	**− 4.84 (10.74)***	− 13.34 (11.38)	− 22.13 ± 1.74
	R	− 3.53 (9.12)*	− 9 (15.47)		
ROM of ankle FE stance (°)	L	22.66 (6.33)	**27.55 (6.53)**	25.38 (6.56)	
	R	23.89 (7)	**28.48 (7.22)**		
ROM of ankle FE swing (°)	L	8.85 (2.36)*	**12.57 (3)**	14.66 (6.16)	
	R	8.93 (2.9)*	**14.05 (7.01)**		
Knee flexion at initial contact (°)	L	31.17 (19.79)*	**28 (16.81)***	1.75 (3.36)	0.99 ± 1.0
	R	29.7 (14.28)*	25.17 (15.45)*		
Min FE of knee (°)	L	11.70 (21)*	13.12 (14.86)*	0.32 (2.37)	
	R	18.35 (9.63)*	15.3 (15.59)*		
ROM of knee FE (°)	L	44.93 (24.31)*	50.07 (22.01)*	66.31 (3.30)	75.52 ± 1.52
	R	41.04 (10.39)*	47.01 (15.72)*		
Min FE of hip (°)	L	15.76 (13.84)*	**11.72 (17.04)***	− 5.05 (12.11)	− 8.18 ± 5.34
	R	17.21 (9.55)*	**6.79 (11.49)***		
ROM of hip FE (°)	L	39.49 (14.12)	**42.02 (9.74)**	41.07 (5.85)	48.75 ± 0.96
	R	36.3 (11.82)	**43.93 (12.71)**		
ROM of hip ABAD (°)	L	18.51 (8.02)	17.86 (4.1)	17.22 (2.79)	
	R	15.32 (6.11)	**16.75 (8.56)**		
ROM of pelvic tilt (°)	L	7.41 (4.54)*	**8.42 (5.32)***	3.60 (0.94)	5.31 ± 0.30
	R	6.78 (3.93)*	**7.96 (5.13)***		
ROM of pelvic obliquity (°)	L	9.94 (6.59)	**13.27 (7.25)**	10.89 (1.54)	
	R	9.88 (6.48)	**13.04 (7.33)**		

Bold at T1 identifies significant differences between patients at T0 and at T1 ($p < 0.05$, Wilcoxon test).
ROM range of motion, *FE* flexo-extension, *ADAB* adb-adduction.
*Indicates significant differences between patients and healthy adults ($p < 0.05$, Mann–Whitney test).

improvement of the GMFM-88 score ($r^2 = 0.682$, F Anova 5.894, $p = 0.009$), as described in Eq. (1) with a main effect of age and cognitive competences ($r^2 = 0.681$, F Anova 8.542, $p = 0.003$), as described in Eq. (2).

$$\text{GMFM-88}_{\text{T1}-\text{T0}} = -0.07\text{GMFCS} + 0.07\text{vIQ} - 0.08\text{pIQ} - 0.29\text{age} + 4.08 \quad (1)$$

$$\text{GMFM-88}_{\text{T1}-\text{T0}} = 0.07\text{vIQ} - 0.08\text{pIQ} - 0.30\text{age} + 3.96 \quad (2)$$

As to GMFM dimensions, age and cognitive competences predicted the change of dimension D ($r^2 = 0.515$, F Anova 4.250, $p = 0.029$, Eq. (3)) and E ($r^2 = 0.667$, F Anova 8.006, $p = 0.003$, Eq. (4)) but not the others. Age was a predictor of the pre–post treatment change detected *via* the FAQ ($r^2 = 0.330$, F Anova 6.903, $p = 0.02$), as described in Eq. (5). The 6MWT was not predicted by the model.

$$\text{GMFM-D}_{\text{T1}-\text{T0}} = 0.14\text{vIQ} - 0.17\text{pIQ} - 0.77\text{age} + 10.87 \quad (3)$$

$$\text{GMFM-E}_{\text{T1}-\text{T0}} = 0.16\text{vIQ} - 0.18\text{pIQ} - 0.81\text{age} + 10.25 \quad (4)$$

$$\text{FAQ}_{\text{T1}-\text{T0}} = -0.1\text{age} + 1.22 \quad (5)$$

The *post hoc* power analysis identified that there is a probability of 75% that the study detects a treatment difference of a two-sided 0.05 significance level.

DISCUSSION

Our group of ambulatory children with bilateral CP was quite similar to those previously described both as to clinical characteristics and to neurocognitive profiles (see Refs. 6,35). General cognitive competencies were overall borderline, though quite inhomogeneous across cognitive domains and subjects, and unrelated to gross motor level of impairment. Coherently with previous data, verbal competences exceeded non-verbal ones, because of greater impairment in visuo-perceptual and constructive skills.[14,32,36]

The intervention performed in immersive virtual reality proved to be effective in our participants, with an overall improvement of the walking competence, as testified by functional and instrumental parameters. The instrumental data detected by the Gait analysis modified their characteristics tending towards the pattern of typically developing children and healthy adults. These results confirm what has been recently described by van Gelder *et al.*[40] in a single session experiment with a group of ambulatory CP participants very similar as to age and to motor impairment to ours. Their experiment could be in some sense considered as preliminary to ours. We proposed a 4-week training in the immersive reality environment and asked our CP children just to walk in a relatively free manner; we therefore let each of them find his/her proper pace, thus regulating and modifying the walking performance according to the efficacy of the free movement. The situation was ecological and somewhat similar to real life, even though the virtual reality environment urged to modification by providing feedback of the performance. The walking performance of our participants improved also as to kinematic parameters (as in Van Gelder *et al.*[40]) also without providing specific real-time feedback for the range of motion. Taken together, our data and those of van Gelder's *et al.* show how the immersive reality environment could help in improving the walking pattern both as a whole competence and as to control of more local levels. Moreover, the intervention in immersive virtual reality proved to be effective also with previously treated preadolescents.

Indeed, the introduction of Virtual Reality in motor rehabilitation for children with CP could help in sustaining motivation and providing multilevel feedback, which in turn could lead to change and modification avoiding dropouts thanks to the engagement in the activity. Though artificial, the experience is more ecological; the successful performance requires improvements of motor-perceptual integration, planning and strategies (see also the work by Yu *et al.*[42]). The resulting performance is thus a combination of multilevel processes among which we find the specific aspects of the motor performance.

Some considerations can be put forward especially considering the possibility to pursue similar goals by using different devices, which are often markedly less expensive. In real-life settings and in traditional therapy situations the feedback relies on the patient's own perception, on the effect of the performance (if a meaningful activity is provided) and mostly on the guide of the therapist. Repetition is needed and the context is adapted as far as possible. VR contexts offer the possibility to propose a meaningful activity and to provide an online feedback both at intrinsic and extrinsic level. The similar-real life context can be quite easily adapted to the individual characteristics, while motivation to practice through repetition is supported by the VR context. These features were provided in our pilot study by the expensive GRAIL system, and were putatively the basis of the detected improvement. Were these data confirmed by larger samples and studies, other cheaper VR systems could be implemented maybe at portable and even domestic levels.

Finally we looked for predictors of the improvement of gross motor competences after the treatment. It is not surprising that general cognitive abilities (verbal/nonverbal components of IQ) together with age were the main predictors with a minor effect of the level of impairment (as by GMFCS level). Motivation, attention together with cognitive engagement are then crucial factors and could determine the improvement of the motor performance, though within the constraints of the clinical pattern. As proposed in a previous study of our group (where new technologies were combined with virtual reality in a treatment focused on upper limb),[36] these findings could depose for the improvement of the strategies used by our participants.

In conclusions, though preliminary and in a small but quite homogeneous group of diplegic children, we highlighted the efficacy of a walking-focused treatment in immersive VR in preadolescents affected by a chronic pathology. The intervention we proposed is highly motivating as well as tolerated, as testified by the absence of drop outs among our already treated preadolescent participants, hence probably more at risk of giving up. We underline how the modifiability of the gait pattern persists along developmental age also in CP, at least up to 16 years as the oldest of our participants, as already suggested in a similar recent study by Van Gelder *et al.*[40] The possibility of modification at least partially relies on learning processes that are active all along development and benefit from stimulation, as testified by the main correlation with age and cognitive abilities (at least in ambulatory children as ours).

Furthermore, while other treatments—even high tech ones such as robot-aided rehabilitation interventions—often do not modify the gait pattern but only gross motor abilities, this treadmill training in immersive VR showed interesting advantages in the rehabilitation of this chronic pathology. Indeed robotic interventions (such as Lokomat by Hocoma) improve GMFM parameters (Dimension D and E) and endurance—though differently across studies; their efficacy on spatiotemporal parameters and kinematics/kinetics—as detected by Gait analysis—is controversial and not significant in the unique randomized control trial on a group of children with CP.[11] Similar data have been reported across different temporal frequency and protocols.[29]

In our study, not only endurance and functional activities improved, but also spatio-temporal and some parameters describing kinematics and kinetics. The changes of GMFM parameters were clearly above minimum clinical significance in dimension E (running, jumping capacity) and significant though more variable in dimension D (standing capacity), whose baseline score was already quite elevate. Comparing the improvements of the CP participants to those obtained in patients with ABI we described in a previous paper,[4] we observed progresses in similar parameters but with different baselines and smaller pre/post changes in functional scales. In contrast, concerning the gait pattern, CP children showed progresses also at the hip and ankle level. These data support the fact that the natural history, recovery and neuroplastic processes are very different in CP and ABI, notwithstanding they may show a similar neurological impairment.

Finally we stress how the improvements we detected are congruent across outcome indexes and are likely to be due to the intervention and not to developmental trajectories, given both age (not so young) and previous treatments. The absence of a control group and follow up limits our conclusions. Still we underline how the immersive VR context could foster integration of motor/perceptual competences beyond the training of the walking ability, giving a chance of improvement also to older and already treated children. The possibility to experiment and modify the performance in an ecological context could underlie the improvement we detected. The enhancement of the technological level will likely support the diffusion and price decrease of these kind of devices that could become essential part of future rehabilitation programs.

CLINICAL MESSAGE

- Cerebral Palsy is a multidimensional and chronic pathology where interventions need to be carefully planned on the basis of evidence.
- New technologies as immersive virtual reality offer the possibility to couple effective interventions with motivation and enhanced use of feedback in an ecological (though artificial) environment.
- The immersive reality environment could help in improving the walking pattern both as a whole competence and as to control of more local levels.
- The intervention in IVR is effective also in previously otherwise treated CP preadolescents.

REFERENCES

[1] Andersson, C., L. Asztalos, and E. Mattsson. Six-minute walk test in adults with cerebral palsy. A study of reliability. *Clin. Rehabil.* 20:488–495, 2006.

[2] Bax, M., M. Goldstein, P. Rosenbaum, A. Leviton, N. Paneth, B. Dan, B. Jacobsson, D. Damiano, and Executive Committee for the Definition of Cerebral Palsy. Proposed definition and classification of cerebral palsy, April 2005. *Dev. Med. Child Neurol.* 47(571–576):2005, 2005.

[3] Beltran, E. J., J. B. Dingwell, and J. M. Wilken. Margins of stability in young adults with traumatic transtibial amputation walking in destabilizing environments. *J. Biomech.* 47:1138–1143, 2014.

[4] Biffi, E., E. Beretta, A. Cesareo, C. Maghini, A. C. Turconi, G. Reni, and S. Strazzer. An immersive virtual reality platform to enhance walking ability of children with acquired brain injuries. *Methods Inf. Med.* 56(2):119–126, 2017.

[5] Bohannon, R. W., and M. B. Smith. Interrater reliability of a modified Ashworth scale of muscle spasticity. *Phys. Ther.* 67:206–207, 1987.

[6] Bottcher, L. Children with spastic cerebral palsy, their cognitive functioning, and social participation: a review. *Child. Neuropsychol.* 16:209–228, 2010.

[7] Cameirao, M. S., S. B. Badia, E. Duarte, A. Frisoli, and P. F. Verschure. The combined impact of virtual reality neurorehabilitation and its interfaces on upper extremity functional recovery in patients with chronic stroke. *Stroke* 43:2720–2728, 2012.

[8] Cho, C., W. Hwang, S. Hwang, and Y. Chung. Treadmill training with virtual reality improves gait, balance, and muscle strength in children with cerebral palsy. *Tohoku J. Exp. Med.* 238:213–218, 2016.

[9] Damiano, D. L., K. E. Alter, and H. Chambers. New clinical and research trends in lower extremity management for ambulatory children with cerebral palsy. *Phys. Med. Rehabil. Clin. N. Am.* 20:469–491, 2009.

[10] Darter, B. J., and J. M. Wilken. Gait training with virtual reality-based real-time feedback: improving gait performance following transfemoral amputation. *Phys. Ther.* 91:1385–1394, 2011.

[11] Druzbicki, M., W. Rusek, S. Snela, J. Dudek, M. Szczepanik, E. Zak, J. Durmala, A. Czernuszenko, M. Bonikowski, and G. Sobota. Functional effects of robotic-assisted locomotor treadmill therapy in children with cerebral palsy. *J. Rehabil. Med.* 45:358–363, 2013.

[12] Druzbicki, M., W. Rusek, M. Szczepanik, J. Dudek, and S. Snela. Assessment of the impact of orthotic gait training on balance in children with cerebral palsy. *Acta Bioeng. Biomech.* 12:53–58, 2010.

[13] Fung, J., C. L. Richards, F. Malouin, B. J. McFadyen, and A. Lamontagne. A treadmill and motion coupled virtual

reality system for gait training post-stroke. *Cyberpsychol. Behav*. 9:157–162, 2006.

[14] Gagliardi, C., A. Tavano, A. C. Turconi, and R. Borgatti. Sequence memory skills in spastic bilateral cerebral palsy are age independent as in normally developing children. *Disabil. Rehabil*. 35:506–512, 2013.

[15] Geijtenbeek, T., F. Steenbrink, B. Otten, and O. Even-Zohar. D-flow: immersive virtual reality and real-time feedback for rehabilitation. Proceedings of the VRCAI 2011, 2011, pp. 201–208.

[16] Gutierrez, R. O., F. Galan Del Rio, R. Cano de la Cuerda, I. M. Alguacil Diego, R. A. Gonzalez, and J. C. Page. A telerehabilitation program by virtual reality-video games improves balance and postural control in multiple sclerosis patients. *NeuroRehabilitation* 33:545–554, 2013.

[17] Hak, L., H. Houdijk, P. van der Wurff, M. R. Prins, A. Mert, P. J. Beek, and J. H. van Dieen. Stepping strategies used by post-stroke individuals to maintain margins of stability during walking. *Clin. Biomech. (Bristol, Avon)* 28:1041–1048, 2013.

[18] Kaufman, K. R., M. P. Wyatt, P. H. Sessoms, and M. D. Grabiner. Task-specific fall prevention training is effective for warfighters with transtibial amputations. *Clin. Orthop. Relat. Res*. 472:3076–3084, 2014.

[19] Lamontagne, A., J. Fung, B. J. McFadyen, and J. Faubert. Modulation of walking speed by changing optic flow in persons with stroke. *J. Neuroeng. Rehabil*. 4:22, 2007.

[20] Luna-Oliva, L., R. M. Ortiz-Gutierrez, R. Cano-de la Cuerda, R. M. Piedrola, I. M. Alguacil-Diego, C. Sanchez-Camarero, and C. Martinez Culebras Mdel. Kinect Xbox 360 as a therapeutic modality for children with cerebral palsy in a school environment: a preliminary study. *NeuroRehabilitation* 33:513–521, 2013.

[21] McAndrew, P. M., J. B. Dingwell, and J. M. Wilken. Walking variability during continuous pseudo-random oscillations of the support surface and visual field. *J. Biomech*. 43:1470–1475, 2010.

[22] Meyer-Heim, A., C. Ammann-Reiffer, A. Schmartz, J. Schafer, F. H. Sennhauser, F. Heinen, B. Knecht, E. Dabrowski, and I. Borggraefe. Improvement of walking abilities after robotic-assisted locomotion training in children with cerebral palsy. *Arch. Dis. Child*. 94:615–620, 2009.

[23] Mutlu, A., K. Krosschell, and D. G. Spira. Treadmill training with partial body-weight support in children with cerebral palsy: a systematic review. *Dev. Med. Child Neurol*. 51:268–275, 2009.

[24] Novacheck, T. F., J. L. Stout, and R. Tervo. Reliability and validity of the Gillette Functional Assessment Questionnaire as an outcome measure in children with walking disabilities. *J. Pediatr. Orthop*. 20:75–81, 2000.

[25] Oeffinger, D., A. Bagley, S. Rogers, G. Gorton, R. Kryscio, M. Abel, D. Damiano, D. Barnes, and C. Tylkowski. Outcome tools used for ambulatory children with cerebral palsy: responsiveness and minimum clinically important differences. *Dev. Med. Child Neurol*. 50:918–925, 2008.

[26] O'Neil, R. L., R. L. Skeel, and K. I. Ustinova. Cognitive ability predicts motor learning on a virtual reality game in patients with TBI. *NeuroRehabilitation* 33:667–680, 2013.

[27] Palisano, R., P. Rosenbaum, S. Walter, D. Russell, E. Wood, and B. Galuppi. Development and reliability of a system to classify gross motor function in children with cerebral palsy. *Dev. Med. Child Neurol*. 39:214–223, 1997.

[28] Palisano, R. J., L. A. Chiarello, M. Orlin, D. Oeffinger, M. Polansky, J. Maggs, A. Bagley, G. Gorton, and Children's Activity and Participation Group. Determinants of intensity of participation in leisure and recreational activities by children with cerebral palsy. *Dev. Med. Child Neurol*. 53:142–149, 2011.

[29] Peri, E., A. C. Turconi, E. Biffi, C. Maghini, D. Panzeri, R. Morganti, A. Pedrocchi, and C. Gagliardi. Effects of dose and duration of robot-assisted gait training on walking ability of children affected by cerebral palsy. *Technol. Health Care* 25(4):671–681, 2017.

[30] Rosie, J. A., S. Ruhen, W. A. Hing, and G. N. Lewis. Virtual rehabilitation in a school setting: is it feasible for children with cerebral palsy? *Disabil. Rehabil. Assist. Technol*. 10:19–26, 2015.

[31] Sessoms, P. H., M. Wyatt, M. Grabiner, J. D. Collins, T. Kingsbury, N. Thesing, and K. Kaufman. Method for evoking a trip-like response using a treadmill-based perturbation during locomotion. *J. Biomech*. 47:277–280, 2014.

[32] Sigurdardottir, S., A. Eiriksdottir, E. Gunnarsdottir, M. Meintema, U. Arnadottir, and T. Vik. Cognitive profile in young Icelandic children with cerebral palsy. *Dev. Med. Child Neurol*. 50:357–362, 2008.

[33] Sloot, L. H., J. Harlaar, and M. M. van der Krogt. Self-paced versus fixed speed walking and the effect of virtual reality in children with cerebral palsy. *Gait Posture* 42:498–504, 2015.

[34] Sloot, L. H., M. M. van der Krogt, and J. Harlaar. Self-paced versus fixed speed treadmill walking. *Gait Posture* 39:478–484, 2014.

[35] Stadskleiv, K., R. Jahnsen, G. L. Andersen, and S. von Tetzchner. Neuropsychological profiles of children with cerebral palsy. *Dev. Neurorehabil* 2017. https://doi.org/10.1080/17518423.2017.1282054.

[36] Turconi, A. C., E. Biffi, C. Maghini, E. Peri, F. Servodio Iammarone, and C. Gagliardi. Can new technologies improve upper limb performance in grown-up diplegic children? *Eur. J. Phys. Rehabil. Med*. 52:672–681, 2016.

[37] van den Bogert, A. J., T. Geijtenbeek, O. Even-Zohar, F. Steenbrink, and E. C. Hardin. A real-time system for biomechanical analysis of human movement and muscle function. *Med. Biol. Eng. Comput*. 51:1069–1077, 2013.

[38] van der Krogt, M. M., L. H. Sloot, A. I. Buizer, and J. Harlaar. Kinetic comparison of walking on a treadmill versus over ground in children with cerebral palsy. *J. Biomech*. 48:3577–3583, 2015.

[39] van der Krogt, M. M., L. H. Sloot, and J. Harlaar. Overground versus self-paced treadmill walking in a virtual environment in children with cerebral palsy. *Gait Posture* 40:587–593, 2014.

[40] van Gelder, L., A. T. Booth, I. van de Port, A. I. Buizer, J. Harlaar, and M. M. van der Krogt. Real-time feedback to improve gait in children with cerebral palsy. *Gait Posture* 52:76–82, 2017.

[41] Wechsler, D. Wechsler Intelligence Scale for Children Revised. New York: Psychological Corporation, 1974.

[42] Yu, Y., and T. A. Stoffregen. Postural and locomotor contributions to affordance perception. *J. Mot. Behav*. 44:305–311, 2012.