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Effectiveness of virtual reality on functional mobility during treadmill training in children with cerebral palsy: a single-blind, two-arm parallel group randomised clinical trial (VirtWalkCP Project)

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ABSTRACT

Introduction Treadmill training and virtual reality have been investigated in children with cerebral palsy. However, few studies have assessed the effectiveness of the combination of both treatments on children's functional and balance activities. The project aims to compare the effects of treadmill training with and without virtual reality on walking endurance and speed, static and dynamic balance, gross motor function, functional independence, quality of life and occupational participation in children with spastic cerebral palsy between the ages of 4 and 12 years classified at levels I, II and III of the Gross Motor Function Classification System.

Methods and analysis This study is a single-blind, two-arm parallel group, randomised, controlled clinical trial. Participants will be recruited at the Pediatric Department of the Vic Hospital Consortium, and the research will be conducted at the University of Vic – Central University of Catalonia. The participants will be randomly allocated into two groups: (1) the experimental group, which will receive the treadmill training at the same time as the virtual reality; and (2) the control group, which will undertake treadmill gait training alone. The training will be provided in 10 sessions over 2 weeks with 30 min for each session. Assessments will be performed on three occasions: 1 week before the intervention, 1 week following the intervention and 1 month after the end of the intervention. The evaluations will involve the 6 min walk test, stabilometry, the Berg Balance Scale, the 10 m walk test, the Gross Motor Function Measure, the Functional Independence Measure, the paediatric quality of life inventory and the Children Participation Questionnaire. For between-within group comparison, a mixed-effect linear model will be used.

Ethics and dissemination The study has been approved by the Clinical Research Ethics Committee of the Osona Foundation for Health Research and Education (2021061). Results will be published in peer-reviewed journals and presented at international conferences.

Trial registration number NCT05131724.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This single-blinded, two-arm parallel group randomised, controlled clinical trial will compare an intensive treadmill training and its combination with virtual reality for children with spastic cerebral palsy.
⇒ Children between 4 and 12 years will be recruited, with a medical diagnosis of spastic cerebral palsy and motor function classified at level the I, II or III by the Gross Motor Function Classification System.
⇒ Children at the treadmill training group will also receive intensive training, which may potentially influence the results regarding the effectiveness of the treadmill training and virtual reality combination.
⇒ Due to the nature of the intervention, the therapist delivering the interventions and participants will not be blinded to allocation.

BACKGROUND

Cerebral palsy (CP), which occurs as a consequence of brain damage, has multiple deficits, such as a global reduction of cortical motor activity during movement execution and inadequate processing of corticospinal and somatosensory circuits.[1–5] Global registers estimate that it occurs in two to three per 1000 live births,[6] and spasticity is the most common disorder, occurring in 80% of children with CP.[6–10] Spasticity might affect both upper and lower limbs, resulting in other deficits in joint mobility, postural reactions, selective motor control, balance and gait.[9 10] This set of impairments and deficits may lead to limitations in functional ability and autonomy in the performance of daily living activities, physical fitness, quality of life and/or ability to participate in games and sports activities compared with neurotypical peers of the same age.[9 11 12] Walking is

considered one of the most important activities in daily life, as it is essential for activities of daily living and social participation.[13] Children with Gross Motor Function Classification System (GMFCS) levels I, II and III show potential for walking.[8 14] On average, 50% of children are ambulatory independently and 20% walk with aids.[15–17] However, abnormalities in neural control and muscle weakness contribute to several gait characteristics, such as slow velocity, decreased stride length, increased stance phase percentage, increased peak ankle dorsiflexion and knee flexion and peak hip extension moments.[18] Consequently, this gait pattern contributes to postural instability and increased fall risk in children with CP, among others.[19 20]

Treadmill training

In recent years, many intervention approaches have been studied to improve selective motor control, sensorimotor cortical activation and muscle coordination during walking in children with CP.[21] Moreover, task-specific training with multiple repetitions and the child's active participation has been shown to promote best the improvement of motor skills.[22–24]

Treadmill gait training has been used to improve gait performance in children with CP.[24–26] Although research in this field is still at an early stage, encouraging results have been demonstrated in children of different ages (between 4 and 18 years) and with levels I–IV of the GMFCS.[24–30] The treadmill can be used with or without partial weight-bearing to provide task-specific training with multiple repetitions of gait cycle steps.[31 32] This method is considered to activate the central generators of movement patterns in the lumbar region of the spinal cord[31 33] which, according to some research, might be altered in children with CP.[34] Therefore, the activation of these generators and automatic reciprocation mechanisms might be essential during treadmill gait stimulation.[30 35]

Several studies state that this training is safe for these children.[24 26 32 36 37] Moreover, moderate and low-quality evidence concludes that treadmill gait training without body weight support increases walking speed and gross motor function, compared with no walking training.[24] However, recent systematic reviews highlight the lack of randomised clinical trials in the CP population and high methodological quality.[24 26 33 36–38]

Virtual reality (VR)

The (re)habilitation approach based on motor learning theory is based on intensive intervention with high task repetitions.[39 40] Motor learning also improves when the task is meaningful, specific and repetitive and when the task difficulty is increased over time.[39 40] In this regard, in recent decades, technologies have been introduced to address the challenges of incorporating these motor learning principles into clinical applications.[41] VR is an interactive experience that occurs in real time and is considered an effective tool for motivating children with CP.[41–44] Depending on the intensity and quality of stimuli elicited by the virtual environments, VR can be differentiated as: (a) non-immersive VR, when the person is not fully immersed in the virtual world but is displayed on computer monitors or television screens; and (B) immersive VR, when the person has the sensation of being present in the virtual world, as he or she is fully immersed in it by a specialised hardware, such as virtual glasses.[45]

In non-immersive VR, the person can simultaneously experience the real world (the physical environment) and the virtual content through an avatar within the game that reproduces the participant's movement using a sensor located on the television that captures the movements and displays them on the screen.[45] This virtual feedback generates positive reinforcement, facilitating the practice and improvement of exercises.[46] VR offers enriched environments that positively affect motor and cognitive performance.[47] Specifically, VR systems allow us to add feedback, challenge and personalisation to the practice. It can provide immediate visual and auditory feedback related to task performance or results, providing children with opportunities to optimise motor learning, which can later lead to neuroplasticity changes.[39 41 48–51] VR systems can provide an ecologically valid environment similar to the real world so children can perform task-specific practices, increasing the duration, intensity and frequency of those practices.[41 48] Finally, task difficulty can be easily adjusted in VR systems to provide sufficient challenge for a child while playing.[41 48 49] In conclusion, VR systems can introduce game features to increase children's motivation, enjoyment and engagement during playing.[49–51]

VR therapy has been used in many fields, such as posture and balance rehabilitation and motor rehabilitation in children with CP.[52 53] In 2012, practical guidelines for VR use in treating children aged 4–17 years with CP were published.[52] Recently, some studies have shown improvement in postural control, balance, upper limb function, muscle strength, visuoperceptual ability, selective motor control and gait in children with CP.[46 48 52 54 55] However, few studies have investigated the application of VR in treadmill gait training for children with CP.[42 43 56]

The primary aim of the proposed project is to perform a comparative analysis of the effects of treadmill training with and without VR on walking endurance and speed, static and dynamic balance, gross motor function, functional independence, quality of life and occupational participation in children with spastic cerebral palsy between the ages of 4 and 12 years classified at levels I, II and III of the GMFCS. The research question can be framed as follows: (P) population: children with CP between 4 and 12 years; (I) intervention: an intensive treadmill training programme while using VR; (C) comparison group: an intensive treadmill training programme; (O) outcome of interest: effectiveness on walking endurance and speed, static and dynamic balance, gross motor function, functional independence, quality of life and occupational participation; and (T) time: training 2 weeks, plus follow-up at week 4.

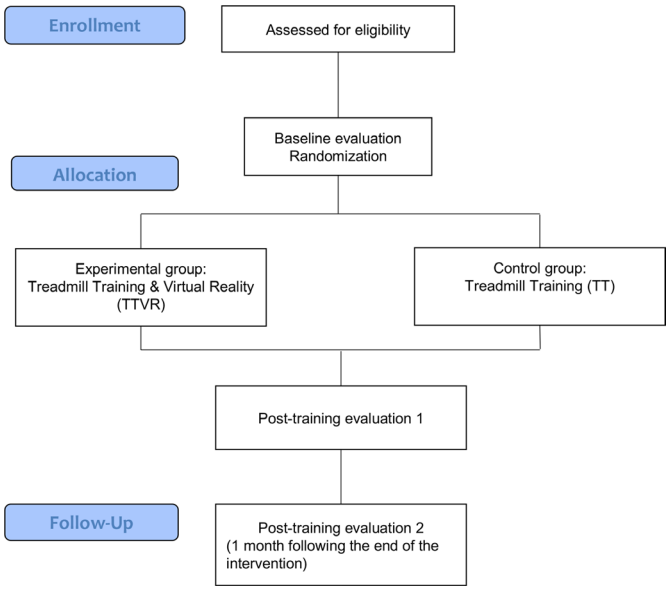

Figure 1 Flow chart.

Authors hypothesise that the combination of VR and treadmill training will achieve more significant effects than the isolated use of treadmill training concerning walking endurance and speed, static and dynamic balance, gross motor function, functional independence, quality of life and occupational participation in children with spastic cerebral palsy between the ages of 4 and 12 years classified at levels I, II and III of the GMFCS.

METHODS/DESIGN

Study design

A prospective, analytical, controlled, randomised, two-arm, single-blinded study will be carried out (figure 1). The protocol for this study is registered at clinicaltrials.org (NCT05131724), and the corresponding Clinical Research Ethics Committee of the Osona Foundation for Health Research and Education (FORES) has approved the study design and protocol (2021061).

The participants will be selected and recruited by the head of the Pediatrics Department at the Pediatric Department of the Vic Hospital Consortium, Catalonia, Spain. The study will be conducted between September 2023 and December 2024. Participants will be randomly allocated into two groups: the control group will undertake treadmill gait training only (TT), and the experimental group will receive the treadmill training at the same time as the virtual reality (TTVR). Both groups will carry out 10 sessions of gait training over 2 weeks, with 30 min for each session at the physiotherapy laboratory of the University of Vic – Central University of Catalonia (UVic-CUC). Outcomes will be collected for both groups at baseline, at the end of the training and 4 weeks after the end of the training.

Randomisation will be stratified based on the GMFCS (level I, II or III), at a ratio of 1:1 for both groups. A randomisation table will be used for the allocation sequence at each stratum. An external researcher not involved in the recruitment process or development of the study will prepare opaque envelopes for each of the three strata (each of different colours), which will be sequentially numbered and contain the name of the assigned group (TTVR or TT). The allocation process will take place following the basal evaluation.[57]

A series of numbered, sealed, opaque envelopes will be used to ensure concealed allocation. Each envelope will contain a card stipulating the name of the group to which the child will be allocated.[57]

Participants

The participants will be selected and recruited based on the following eligibility criteria: children aged between 4 and 12 years, with a medical diagnosis of spastic CP by a paediatric neurologist, motor function classified at level I, II or III by the GMFCS,[8] with independent walk acquired for more than 12 months and able to ambulate for at least 10 metres with or without the need for a gait-assistance device (walker or crutches).

Exclusion criteria include orthopaedic surgery on the lower limbs in the past 12 months, surgery scheduled during the period of the study, orthopaedic deformities with the indication for surgery, uncontrolled seizure disorder, metallic implant in the skull or hearing aid, having received botulinum toxin injections in the 6 months before the start of the study and cognitive or visual alterations that may compromise task performance.

The sample size was calculated using the G*Power 3 Software based on differences between two independent groups. The 6 min walk test was selected as the primary outcome due to its proven validity and reliability as a functional capacity assessment tool and will be used to assess participants' walking endurance and functional mobility. Based on the results of Grecco *et al*,[27] and considering a mean and SD of 377.2±93.0 m in the experimental group and 268±45 m in the control group, a Cohen's d effect size of 1.49 was obtained. Considering an alpha error of 0.05 and power at 95%, a sample size of 13 participants per group was obtained. The drop-out rate was set at 15% of the required subjects, so the total sample size will be 30 participants (15 per group).

Patient and public involvement

No patient was involved.

Data collection

The children in both groups will be evaluated by two physiotherapists, trained to perform the evaluations beforehand, experienced with the evaluation procedures and blinded to the allocation of the children to the different groups. Three evaluations will be carried out:

- Baseline evaluation: 1 week before the training.
- Post-training evaluation 1: at the end of the training.
- Post-training evaluation 2: 4 weeks after the end of the training.

Table 1 Summary of the outcomes and measurements

Outcome	Type of outcome	Outcome measure
Body function-based measures		
Walking endurance	Primary outcome	6MWT
Static balance	Secondary outcome	Stabilimeter platform
Dynamic or functional balance	Secondary outcome	Berg Balance Scale
Walking speed	Secondary outcome	10MWT
Activity-based measures		
Gross motor function	Secondary outcome	GMFM-66_IS
Functional independence	Secondary outcome	WeeFIM
Participation-based measures		
Quality of life	Secondary outcome	PedsQoL
Occupational participation	Secondary outcome	CPQ

CPQ, Children Participation Questionnaire; GMFM-66 IS, Gross Motor Function Measure-66 Item set; 6MWT, 6 min walk test; 10MWT, 10 m walk test; PedsQoL, Pediatrics Quality of Life Inventory; WeeFIM, Functional Independence Measure for Children.

At baseline, each participant will be assessed with demographic details such as age, GMFCS level, age of independent gait acquisition, history of orthopaedic surgery and upcoming planned surgeries. Also, a battery of comprehensive measurements of primary and secondary outcome measures will be completed based on the International Classification of Functioning, Disability and Heald for Children and Youth and previous literature[58] (table 1).

Outcome measures

The primary outcome measure includes body function-based measures. Walking endurance will be assessed by the 6 min walk test (6MWT), which will be performed in accordance with recommendations.[59] Physiological variables such as heart rate and oxygen saturation will be collected using a wireless wrist pulse oximeter (BCOxygen Oxysleep). The test will be performed once in a 10 m course layout. Participants will receive standardised instructions and encouragement. The test–retest interclass correlation coefficient of this test is 0.98.[59–61] The estimated time to perform the test is 10 min.

The secondary outcome measures include three major outcomes: the body functions-based measures, the activity-based measures, and the participation-based measures.

The static balance will be assessed on a stabilimeter platform (System SD – Biodex), which allows stabilometric analysis based on oscillations of the centre of pressure. The children will be instructed to remain standing on the platform, barefoot, arms alongside the body, gazed fixed on a point that will appear on the platform's integrated screen (at eye level, adjusted for each child), with the base of the foot free and heels aligned. The platform also has support rails if the participant loses balance during the test and needs to hold on. Readings will be taken for 30 s in two conditions (eyes open and eyes closed). Displacement will be measured from the oscillations of the centre of pressure in the X (anterior-posterior) and Y (medial-lateral) axes in both conditions.[62] The test is estimated to last 5 min.

Dynamic or functional balance will be evaluated by the Berg Balance Scale. This simple 14-item measure addresses the performance of functional balance common to daily living. Each item has a five-option scale ranging from 0 to 4 points, with a maximum overall score of 56. The points are based on the time in which a position is maintained, the distance an upper limb is able to reach in front of the body and the time needed to complete the task.[63] The inter-rater reliability is 0.99, demonstrating the excellent reliability of this instrument.[64] The total execution time is approximately 20 min.

Walking speed will be assessed by the 10 m walk test, which has excellent measurement properties and is a task-specific objective measure of stepping or walking speed within an indoor environment.[65] The test can be completed with or without a gait trainer and is not diagnostic specific.[30 31 36] Children will be instructed to walk 14 m, and their speed will be measured for 10 m to exclude acceleration at the beginning and deceleration at the end of the gait. Physical facilitation for one step will be provided for children that cannot initiate steps within a 30 s time frame.[66] A maximum time of 10 min will be provided to complete the 10 m. A change of 0.1 m/s will be clinically meaningful.[67] The inter-rater reliability of this instrument is very high, between 0.89 and 1.00.[66] The total execution time is approximately 10 min.

Gross motor function will be assessed by the Gross Motor Function Measure-66-item set (GMFM-66-IS). This tool is an updated version of GMFM-66 and is considered accurate, time efficient and suitable for research.[68] This scale quantifies the child's gross motor function in different positions (lying down and rolling, sitting, crawling and kneeling, standing, walking, running and jumping), scoring each item from 0 to 3 points, with higher scores denoting a better performance. Clinically meaningful change for the GMFM in children with CP aged 1.5–7 years old is 1.23 for individuals classified at GMFCS level III.[69 70] The test is estimated to last 10 min.

Functional independence will be evaluated by the Functional Independence Measure for Children (WeeFIM). It has excellent measurement properties to measure consistent performance of activities of daily living, functional independence and burden of care in children with disabilities.[38 71] It is a semistructured interview that is guided by a specific manual to determine the level of assistance

required for: (1) self-care, (2) transfers and mobility, and (3) cognition and communication. A total of 18 items are scored on a scale of 1 (indicating total assistance required for completion of the task) to 7 (complete independence), giving a total score out of 126.[72] The WeeFIM will be completed by the parents or guardians of each child.

Quality of life will be assessed by the Pediatric Quality of Life Inventory (PedsQoL).[73–75] The 23-item scale encompasses: (1) physical functioning (eight items), (2) emotional functioning (five items), (3) social functioning (five items) and (4) school functioning (five items) and will be completed by the parents or guardians of each child. The instructions ask how much problem each item has been during the past month. A 5-point response scale is used (0=never a problem; 1=almost never a problem; 2=sometimes a problem; 3=often a problem; 4=almost always a problem).[74 76]

Occupational participation will be assessed by the Children Participation Questionnaire (CPQ). This questionnaire will be completed by the parents or guardians of each child. It documents the child's participation in six occupational areas: (1) activities of daily living, (2) instrumental activities, (3) play, (4) leisure, (5) social participation and (6) education. Parents will report the intensity of the level of independence and the child's enjoyment and satisfaction. It consists of 44 items scored on a six-point scale (1–6). A higher score is considered as higher enjoyment or satisfaction.[77 78]

All the physical assessments will be video recorded and scored by one of the two experienced physiotherapists, blinded to assessment time points and the allocation of the children to the different groups. Before the evaluation procedures, both physiotherapists will be instructed to use each of the assessment tools. Outcome measures with WeeFim, PedsQoL and CPQ will be collected through the parents or guardians of each child, and in the case of children between 8 and 12 years, those outcome measures will also be collected through them. It is estimated that all the physical assessments will last 60 min, and they will be performed at the physiotherapy laboratory of the UVic-CUC.

All the data will be managed and registered simultaneously by the assessors under the coding number assigned to each participant. All the data will be stored on the servers of the UVic-CUC, which comply with the legally required security standards.

Intervention protocols

The control group will receive treadmill gait training only, and the experimental group will undertake the treadmill training at the same time as the VR.

Treadmill training

Children in both groups will perform treadmill training following recommendations.[79] The RAM870A of the Medisoft treadmill will be used. Two treadmill training sessions will be held before the start of the intervention to familiarise the children with the equipment. During these two sessions, the treadmill training and speed will be set according to the following procedures: the ground walking speed of each child will be determined through the baseline 6MWT, and then the training velocity will be set at 50% of the maximum ground speed established during the 6MWT and increased gradually based on the tolerance of each child (ie, no complaint of fatigue, heart rate not exceeding 70% of the maximum heart rate and a lack of gait shuffling, buckling or dragging steps more than 5 s during walking).[59–61]

When the training begins, the velocity will be gradually increased during the session based on the child's tolerance. The treadmill training would be 10 sessions over 2 weeks with 30 min for each session (5 min warm-up, 20 min gait training, 5 min cool-down).[79] During the sessions, treadmill speed will be maintained at 60%–80% of the maximum speed established on the exertion test. The child will walk at 60% maximum speed in the first and final 5 min and 80% in the middle 20 min.

The physiotherapist conducting the training and the participant's companion will be available to help the child through verbal and tactile feedback to encourage heel strike, hip and knee extension and toe-off. The treadmill structure will have an adjustable handlebar so the child can hold on if needed. In addition, the participant will wear a safety harness and an automatic stop lanyard.

The following criteria will be pre-established for interruption of training: the sensation of fatigue, pain in the lower limbs, complex arrhythmia, increased heart rate above the participant's established maximum, severe shortness of breath and drop in oxygenation. The participant will be asked about the shortness of breath and lower limb pain in all sessions. In addition, heart rate and oxygen saturation will be monitored continuously using a wireless wrist pulse oximeter.

Virtual reality

Children in the experimental group will perform gait training on the treadmill simultaneously with VR (TTVR). The virtual environment will be composed of obstacles, different paths, and narrow and deviated corridors. The child will control an avatar that walks through this environment and requires the child to coordinate walking behaviour and adjust the length, height and width of steps to avoid obstacles. The VR system will use a television screen placed at the child's eye level in front of the treadmill. The speed, orientation, size, frequency of appearance and shape of the obstacles will be manipulated according to individual performance following a standardised protocol. The VR system will provide visual and auditory feedback on the success or failure of the activity to enhance motor learning. In addition, the characteristics of the environment (eg, visibility, configuration and distractions) will be adjusted to increase the complexity of the training. This complexity will also be adjusted to maintain the 80/20 success/failure ratio to enhance motor learning and encourage child's participation in the game without frustrating them.

The motion capture will be performed by a camera and capture sensors placed on the participants' feet to measure movements as they walk on the treadmill. The participants' movements will be transferred to the VR system and projected onto a 50-inch TV screen as an avatar, allowing participants to see a body walking in the virtual environment. The screen will be situated in front of the child, at the level of his/her eyes, as it will be placed on an adjustable platform. All the interventions will be developed at the physiotherapy laboratory of the UVic-CUC. The number of sessions attended, the maximum treadmill training speed, duration of treadmill training and distance travelled in each session will be recorded on a follow-up chart. Any problems or injuries that may occur during training will also be recorded. All participants will be instructed to maintain their usual daily activities and attend regular physical therapy sessions if undergoing such therapy.

Statistical analysis

Clinical and demographic characteristics and baseline data will be presented to show the baseline comparability of the two groups. Data from the patients who withdrew from the study will also be examined. Descriptive statistics will be presented for both groups at every assessment time point. Normally distributed data will be described using means and SD, and not normally distributed data using medians and IQRs. The intention-to-treat principle will be used during the primary analysis, including all randomised participants. Subjects who discontinue the intervention will be encouraged to participate in the follow-up assessments. The primary outcome measure, walking endurance, is a continuous variable. Therefore, between-group mean differences and 95% CIs from pretreatment assessment to post-treatment assessment and 4-week post-treatment assessment will be analysed using a mixed-effects linear model, including a random term representing individual profile variations (random) and the effect of time, group, and the interaction between time and group (fixed). Any detected possible confounders will be assessed and retained as covariables if they are shown to be influential to the model. Secondary outcomes will be analysed using the same method as the primary outcome measures. The statistical analysis will be performed with the IBM SPSS V.28 (IBM).

DISCUSSION

This paper offers a detailed description of a randomised, controlled, blinded, clinical trial aimed at comparing the effects of the combination of VR and treadmill training and treadmill training only on motor function in children with spastic cerebral palsy between the ages of 4 and 12 years classified at levels I, II and III of the GMFCS. The intervention has been designed to be safe and motivational for the participants and based on the dosage and intensity reported to be effective in gait training programmes.[79 80] Treadmill training has been accepted as task-oriented repetitive training based on motor learning theory and has been considered crucial in improving gait patterns in children with CP.[81] Furthermore, this study protocol is innovative in terms of the combination of VR and treadmill training, which might favour children's acceptability and motivation for the intervention. Individualised adaptations might be necessary to ensure the child's individual goals, but every effort will be made to standardise each intervention element. Outcome measures have been selected to represent the ICF-CY domains. The results will be published and will contribute evidence regarding the use of VR and treadmill training on this population.

ETHICS AND DISSEMINATION

The present study complies with the principles of the Declaration of Helsinki and The Organic Law 3/2018 of December 5 on Protection of Personal Data and Guarantee of Digital Rights established in Spain. The Clinical Research Ethics Committee of the Osona Foundation for Health Research and Education (FORES) has approved the study design and protocol (2021061). Written informed consent will be obtained from the parents or guardians of all participants under 16 years old. The participating institutions have provided a declaration of participation. The participants will be allowed to abandon the study at any time with no negative repercussions.

The findings of this research will be submitted for peer-reviewed publication and presented at international conferences. If any harm arises from the study, these results will also be shared. Non-identifiable data will not be shared. All the involved participants and sites will be acknowledged in the research outputs.

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Contributors All authors contributed to the conception and design of the study. MO-A provided the idea for the study, established the hypothesis and wrote the original proposal. MT-M, TFNC, MTR and SG significantly contributed to the drafting of this paper. All the authors were involved in critically revising the manuscript. This protocol paper was written by MO-A and MT-M with input from all co-authors. All authors read and approved the final manuscript.

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Patient consent for publication Consent obtained from parent(s)/guardian(s)

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REFERENCES

1 Almasri NA, Saleh M, Abu-Dahab S, *et al*. Development of a cerebral palsy follow-up registry in Jordan (CPUP-Jordan). *Child Care Health Dev* 2018;44:131–9.
2 Kavcic A, Vodusek DB. A historical perspective on cerebral palsy as a concept and a diagnosis. *Eur J Neurol* 2005;12:582–7.
3 Burton H, Dixit S, Litkowski P, *et al*. Functional connectivity for somatosensory and motor cortex in spastic diplegia. *Somatosens Mot Res* 2009;26:90–104.
4 Shin YK, Lee DR, Hwang HJ, *et al*. A novel EEG-based brain mapping to determine cortical activation patterns in normal children and children with cerebral palsy during motor imagery tasks. *NeuroRehabilitation* 2012;31:349–55.
5 Rose S, Guzzetta A, Pannek K, *et al*. MRI structural connectivity, disruption of primary sensorimotor pathways, and hand function in cerebral palsy. *Brain Connect* 2011;1:309–16.
6 Graham HK, Rosenbaum P, Paneth N, *et al*. Cerebral palsy. *Nat Rev Dis Primers* 2016;2:15082.
7 Vitrikas K, Dalton H, Breish D. Cerebral palsy: an overview. *Am Fam Physician* 2020;101:213–20.
8 Palisano R, Rosenbaum P, Walter S, *et al*. Development and reliability of a system to classify gross motor function in children with cerebral palsy. *Dev Med Child Neurol* 1997;39:214–23.
9 Mutlu A, Büğüşan S, Kara Özgün K. Impairments, activity limitations, and participation restrictions of the International classification of functioning, disability, and health model in children with ambulatory cerebral palsy. *Saudi Med J* 2017;38:176–85.
10 Hägglund G, Lauge-Pedersen H, Wagner P. Characteristics of children with hip displacement in cerebral palsy. *BMC Musculoskelet Disord* 2007;8:101.
11 Bjornson KF, Belza B, Kartin D, *et al*. Ambulatory physical activity performance in youth with cerebral palsy and youth who are developing typically. *Phys Ther* 2007;87:248–57.
12 Fowler EG, Knutson LM, Demuth SK, *et al*. Pediatric endurance and limb strengthening (pedals) for children with cerebral palsy using stationary cycling: a randomized controlled trial. *Phys Ther* 2010;90:367–81.
13 Chiou II, Burnett CN. Values of activities of daily living. A survey of stroke patients and their home therapists. *Phys Ther* 1985;65:901–6.
14 Kamp FA, Lennon N, Holmes L, *et al*. Energy cost of walking in children with spastic cerebral palsy: relationship with age, body composition and mobility capacity. *Gait Posture* 2014;40:209–14.
15 Wu YW, Day SM, Strauss DJ, *et al*. Prognosis for ambulation in cerebral palsy: a population-based study. *Pediatrics* 2004;114:1264–71.
16 Beckung E, Hagberg G, Uldall P, *et al*. Probability of walking in children with cerebral palsy in Europe. *Pediatrics* 2008;121:e187–92.
17 Himmelmann K, Beckung E, Hagberg G, *et al*. Gross and fine motor function and accompanying impairments in cerebral palsy. *Dev Med Child Neurol* 2006;48:417–23.
18 Ma Y, Liang Y, Kang X, *et al*. Gait characteristics of children with spastic cerebral palsy during inclined treadmill walking under a virtual reality environment. *Appl Bionics Biomech* 2019;2019:8049156.
19 Alemdaroğlu E, Özbudak SD, Mandiroğlu S, *et al*. Predictive factors for inpatient falls among children with cerebral palsy. *J Pediatr Nurs* 2017;32:25–31.
20 Chakraborty S, Nandy A, Kesar TM. Gait deficits and dynamic stability in children and adolescents with cerebral palsy: a systematic review and meta-analysis. *Clin Biomech* 2020;71:11–23.
21 Moreau NG, Bodkin AW, Bjornson K, *et al*. Effectiveness of rehabilitation interventions to improve gait speed in children with cerebral palsy: systematic review and meta-analysis. *Phys Ther* 2016;96:1938–54.
22 Novak I, Morgan C, Fahey M, *et al*. State of the evidence traffic lights 2019: systematic review of interventions for preventing and treating children with cerebral palsy. *Curr Neurol Neurosci Rep* 2020;20:3.
23 Morgan C, Darrah J, Gordon AM, *et al*. Effectiveness of motor interventions in infants with cerebral palsy: a systematic review. *Dev Med Child Neurol* 2016;58:900–9.
24 Chiu H-C, Ada L, Bania TA. Mechanically assisted walking training for walking, participation, and quality of life in children with cerebral palsy. *Cochrane Database Syst Rev* 2020;11:CD013114.
25 Ameer MA, Fayez ES, Elkholy HH. Improving spatiotemporal gait parameters in spastic diplegic children using treadmill gait training. *J Bodyw Mov Ther* 2019;23:937–42.
26 Grecco LAC, Hugo P, Sampaio LMM, *et al*. Evidence of the effect of treadmill training on children with cerebral palsy: a systematic review. *Clin Exp Med Lett* 2012;53:RP95–100.
27 Grecco LAC, Tomita SM, Christovão TCL, *et al*. Effect of treadmill gait training on static and functional balance in children with cerebral palsy: a randomized controlled trial. *Braz J Phys Ther* 2013;17:17–23.
28 Cherng R-J, Liu C-F, Lau T-W, *et al*. Effect of treadmill training with body weight support on gait and gross motor function in children with spastic cerebral palsy. *Am J Phys Med Rehabil* 2007;86:548–55.
29 Johnston TE, Watson KE, Ross SA, *et al*. Effects of a supported speed treadmill training exercise program on impairment and function for children with cerebral palsy. *Dev Med Child Neurol* 2011;53:742–50.
30 Willoughby KL, Dodd KJ, Shields N. A systematic review of the effectiveness of treadmill training for children with cerebral palsy. *Disabil Rehabil* 2009;31:1971–9.
31 Mattern-Baxter K. Effects of partial body weight supported treadmill training on children with cerebral palsy. *Pediatr Phys Ther* 2009;21:12–22.
32 Molina-Rueda F, Aguila-Maturana AM, Molina-Rueda MJ, *et al*. Treadmill training with or without partial body weight support in children with cerebral palsy: systematic review and meta-analysis. *Rev Neurol* 2010;51:135–45.
33 Mattern-Baxter K. Locomotor treadmill training for children with cerebral palsy. *Orthop Nurs* 2010;29:165–9.
34 MacKay-Lyons M. Central pattern generation of locomotion: a review of the evidence. *Phys Ther* 2002;82:69–83.
35 Willoughby KL, Dodd KJ, Shields N, *et al*. Efficacy of partial body weight-supported treadmill training compared with overground walking practice for children with cerebral palsy: a randomized controlled trial. *Arch Phys Med Rehabil* 2010;91:333–9.
36 Damiano DL, DeJong SL. A systematic review of the effectiveness of treadmill training and body weight support in pediatric rehabilitation. *J Neurol Phys Ther* 2009;33:27–44.
37 Zwicker JG, Mayson TA. Effectiveness of treadmill training in children with motor impairments: an overview of systematic reviews. *Pediatr Phys Ther* 2010;22:361–77.
38 Mutlu A, Krosschell K, Spira DG. Treadmill training with partial body-weight support in children with cerebral palsy: a systematic review. *Dev Med Child Neurol* 2009;51:268–75.
39 Kleim JA, Jones TA. Principles of experience-dependent neural plasticity: implications for rehabilitation after brain damage. *J Speech Lang Hear Res* 2008;51:225–39.
40 Shishov N, Melzer I, Bar-Haim S. Parameters and measures in assessment of motor learning in neurorehabilitation; a systematic review of the literature. *Front Hum Neurosci* 2017;11:82.
41 Demers M, Fung K, Subramanian SK, *et al*. Integration of motor learning principles into virtual reality interventions for individuals with cerebral palsy: systematic review. *JMIR Serious Games* 2021;9:e23822.
42 Deutsch JE, Borbely M, Filler J, *et al*. Use of a low-cost, commercially available gaming console (Wii) for rehabilitation of an adolescent with cerebral palsy. *Phys Ther* 2008;88:1196–207.
43 Harris K, Reid D. The influence of virtual reality play on children's motivation. *Can J Occup Ther* 2005;72:21–9.
44 Reid D. The influence of virtual reality on playfulness in children with cerebral palsy: a pilot study. *Occup Ther Int* 2004;11:131–44.
45 Georgiev DD, Georgieva I, Gong Z, *et al*. Virtual reality for neurorehabilitation and cognitive enhancement. *Brain Sci* 2021;11:221.
46 Bailey BW, McInnis K. Energy cost of exergaming: a comparison of the energy cost of 6 forms of exergaming. *Arch Pediatr Adolesc Med* 2011;165:597–602.
47 Morgan C, Novak I, Badawi N. Enriched environments and motor outcomes in cerebral palsy: systematic review and meta-analysis. *Pediatrics* 2013;132:e735–46.
48 Chen Y, Fanchiang HD, Howard A. Effectiveness of virtual reality in children with cerebral palsy: a systematic review and meta-analysis of randomized controlled trials. *Phys Ther* 2018;98:63–77.
49 Levac D, Rivard L, Missiuna C. Defining the active ingredients of interactive computer play interventions for children with neuromotor impairments: a scoping review. *Res Dev Disabil* 2012;33:214–23.

50 Abdalla T, Prudence C, Ribeiro M, *et al*. Analysis of the evolution of standing balance in children with cerebral palsy under virtual rehabilitation, aquatic therapy and physiotherapy traditional. *Rev Mov* 2010;3:181–6.
51 Clark RA, Bryant AL, Pua Y, *et al*. Validity and reliability of the Nintendo Wii balance board for assessment of standing balance. *Gait Posture* 2010;31:307–10.
52 Monge Pereira E, Molina Rueda F, Alguacil Diego IM, *et al*. Use of virtual reality systems as proprioception method in cerebral palsy: clinical practice guideline. *Neurologia* 2014;29:550–9.
53 Weiss PL, Rand D, Katz N, *et al*. Video capture virtual reality as a flexible and effective rehabilitation tool. *J Neuroeng Rehabil* 2004;1:12.
54 Bilde PE, Kliim-Due M, Rasmussen B, *et al*. Individualized, home-based interactive training of cerebral palsy children delivered through the Internet. *BMC Neurol* 2011;11:32.
55 Brien M, Sveistrup H. An intensive virtual reality program improves functional balance and mobility of adolescents with cerebral palsy. *Pediatr Phys Ther* 2011;23:258–66.
56 Cho C, Hwang W, Hwang S, *et al*. Treadmill training with virtual reality improves gait, balance, and muscle strength in children with cerebral palsy. *Tohoku J Exp Med* 2016;238:213–8.
57 Doig GS, Simpson F. Randomization and allocation concealment: a practical guide for researchers. *J Crit Care* 2005;20:183–7.
58 Martinuzzi A, De Polo G, Bortolot S, *et al*. Pediatric neurorehabilitation and the ICF. *NeuroRehabilitation* 2015;36:31–6.
59 ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. Ats statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* 2002;166:111–7.
60 Li AM, Yin J, Yu CCW, *et al*. The six-minute walk test in healthy children: reliability and validity. *Eur Respir J* 2005;25:1057–60.
61 Maher CA, Williams MT, Olds TS. The six-minute walk test for children with cerebral palsy. *Int J Rehabil Res* 2008;31:185–8.
62 Nobre A, Monteiro FF, Golin MO, *et al*. Analysis of postural oscillation in children with cerebral palsy. *Electromyogr Clin Neurophysiol* 2010;50:239–44.
63 Kembhavi G, Darrah J, Magill-Evans J, *et al*. Using the Berg balance scale to distinguish balance abilities in children with cerebral palsy. *Pediatr Phys Ther* 2002;14:92–9.
64 Franjoine MR, Gunther JS, Taylor MJ. Pediatric balance scale: a modified version of the Berg balance scale for the school-age child with mild to moderate motor impairment. *Pediatr Phys Ther* 2003;15:114–28.
65 Dodd KJ, Foley S. Partial body-weight-supported treadmill training can improve walking in children with cerebral palsy: a clinical controlled trial. *Dev Med Child Neurol* 2007;49:101–5.
66 Thompson P, Beath T, Bell J, *et al*. Test-Retest reliability of the 10-metre fast walk test and 6-minute walk test in ambulatory school-aged children with cerebral palsy. *Dev Med Child Neurol* 2008;50:370–6.
67 Soper AK, Cross A, Rosenbaum P, *et al*. Knowledge translation strategies to support service providers' implementation of the "F-words in Childhood Disability". *Disabil Rehabil* 2021;43:3168–74.
68 Avery LM, Russell DJ, Rosenbaum PL. Criterion validity of the GMFM-66 item set and the GMFM-66 basal and ceiling approaches for estimating GMFM-66 scores. *Dev Med Child Neurol* 2013;55:534–8.
69 Wong V, Chung B, Hui S, *et al*. Cerebral palsy: correlation of risk factors and functional performance using the functional independence measure for children (WeeFIM). *J Child Neurol* 2004;19:887–93.
70 Ko J. Sensitivity to functional improvements of GMFM-88, GMFM-66, and PEDI mobility scores in young children with cerebral palsy. *Percept Mot Skills* 2014;119:305–19.
71 Ottenbacher KJ, Msall ME, Lyon N, *et al*. The WeeFIM instrument: its utility in detecting change in children with developmental disabilities. *Arch Phys Med Rehabil* 2000;81:1317–26.
72 Peterson MD, Gordon PM, Hurvitz EA. Chronic disease risk among adults with cerebral palsy: the role of premature sarcopoenia, obesity and sedentary behaviour. *Obes Rev* 2013;14:171–82.
73 Varni JW, Seid M, Kurtin PS. PedsQL 4.0: reliability and validity of the pediatric quality of life inventory version 4.0 generic core scales in healthy and patient populations. *Med Care* 2001;39:800–12.
74 Varni JW, Burwinkle TM, Seid M, *et al*. The PedsQL 4.0 as a pediatric population health measure: feasibility, reliability, and validity. *Ambul Pediatr* 2003;3:329–41.
75 Maher CA, Toohey M, Ferguson M. Physical activity predicts quality of life and happiness in children and adolescents with cerebral palsy. *Disabil Rehabil* 2016;38:865–9.
76 González-Gil T, Mendoza-Soto A, Alonso-Lloret F, *et al*. The Spanish version of the health-related quality of life questionnaire for children and adolescents with heart disease (PedsQL(TM)). *Rev Esp Cardiol* 2012;65:249–57.
77 Smits D-W, van Gorp M, van Wely L, *et al*. Participation in social roles of adolescents with cerebral palsy: exploring Accomplishment and satisfaction. *Arch Rehabil Res Clin Transl* 2019;1:100021.
78 Rosenberg L, Jarus T, Bart O. Development and initial validation of the children participation questionnaire (CPQ). *Disabil Rehabil* 2010;32:1633–44.
79 Booth ATC, Buizer AI, Meyns P, *et al*. 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.
80 Grecco LAC, de Almeida Carvalho Duarte N, Mendonça ME, *et al*. Transcranial direct current stimulation during treadmill training in children with cerebral palsy: a randomized controlled double-blind clinical trial. *Res Dev Disabil* 2014;35:2840–8.
81 Nudo RJ, Wise BM, SiFuentes F, *et al*. Neural substrates for the effects of rehabilitative training on motor recovery after ischemic infarct. *Science* 1996;272:1791–4.