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Abstract

Background. Several pilot studies have evoked interest in robot-assisted therapy (RAT) in children with cerebral palsy (CP). **Objective.** To assess the effectiveness of RAT in children with CP through a single-blind randomized controlled trial. **Patients and Methods.** Sixteen children with CP were randomized into 2 groups. Eight children performed 5 conventional therapy sessions per week over 8 weeks (control group). Eight children completed 3 conventional therapy sessions and 2 robot-assisted sessions per week over 8 weeks (robotic group). For both groups, each therapy session lasted 45 minutes. Throughout each RAT session, the patient attempted to reach several targets consecutively with the REAPlan. The REAPlan is a distal effector robot that allows for displacements of the upper limb in the horizontal plane. A blinded assessment was performed before and after the intervention with respect to the International Classification of Functioning framework: body structure and function (upper limb kinematics, Box and Block test, Quality of Upper Extremity Skills Test, strength, and spasticity), activities (Abilhand-Kids, Pediatric Evaluation of Disability Inventory), and participation (Life Habits). **Results.** During each RAT session, patients performed 744 movements on average with the REAPlan. Among the variables assessed, the smoothness of movement ($P < .01$) and manual dexterity assessed by the Box and Block test ($P = .04$) improved significantly more in the robotic group than in the control group. **Conclusions.** This single-blind randomized controlled trial provides the first evidence that RAT is effective in children with CP. Future studies should investigate the long-term effects of this therapy.

Keywords

rehabilitation, robotics, cerebral palsy, kinematics, motor learning, pediatrics, International Classification of Functioning, Disability and Health

Introduction

Cerebral palsy (CP) is a neurodevelopmental disease related to nonprogressive cerebral abnormalities that occur before birth or early in life, and it affects 2 to 3 children out of every 1000.¹ Children with CP children have hemiplegia, quadriplegia, or diplegia, which could be associated with abnormal sensibility, motor control, strength, and tonus (ie, spasticity) of the upper limb.^{2,3} These impairments may restrict the functional capacity and participation in activities of daily living (ADL) of a child with CP.^{4,5}

Recent recommendations state that intensive rehabilitation is necessary for improving motor function in children with CP.^{4,5} These recommendations, based on motor learning theories, suggest that repetitive, goal-directed, assist-as-needed movements that are associated with sensory feedback and an attractive environment are likely to

promote reorganization of the neuronal networks (ie, neuroplasticity) and motor development after brain injuries.^{4,6,7}

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Robot-assisted therapy (RAT) of the upper limb has the potential to satisfy these recommendations in children with CP.⁸⁻¹² RAT is conducted using robotic devices that enable the patients to perform specific upper limb movements.¹² The main interest in using robots is to allow the patients to achieve a large amount of movement in a limited time. For instance, children with CP were able to perform 640 movements during 60-minute RAT sessions.⁸ Additionally, the attractive human-machine interface has the capacity to motivate the child to perform his or her therapy.¹² This visual interface can be adapted to be kid-friendly through playful games, such as car races,^{8,10,11} or to perform exercises that mimic ADL, such as reaching for a cup.¹⁰ Moreover, robotic devices allow the patient to receive visual, auditory, or sensory feedbacks.^{8,11} Finally, the haptic interaction of the robot gives performance-based assistance to the patients.^{13,14} This assistance can enhance the neuronal plasticity by enabling the patients to initiate and accomplish movements as actively as possible.¹³

RAT efficacy has been studied in stroke patients.¹⁵ A recent meta-analysis concluded that RAT could improve upper limb structure and function and the ADL of these patients. Some pilot studies have described the feasibility and interest in using this therapy in children with CP.^{8,10,11,16,17} However, there are no currently published randomized controlled trials, and a recent review has noted that such studies are needed to confirm the usefulness of RAT in children with CP.⁴

Pilot studies have investigated RAT efficacy in place of, but not combined with, conventional therapy (CT).^{8,10,11,16,17} In everyday life, the combination of RAT, involving substantial movement, and CT could enable the therapist to reallocate his or her time and energy to transferring the benefits of these repetitive movements (for instance, motor control improvement in stroke patients)¹⁵ to ADL and patient social integration.

According to these considerations, the purpose of this study was to assess the effectiveness of RAT combined with CT compared to conventional therapy alone in children with CP. This comparison was performed in a single-blind randomized controlled trial. The assessment protocol was in accordance with the 3 International Classification of Functioning (ICF) domains.

Patients and Methods

The ethics board of our Faculty of Medicine approved this study. All parents freely accepted the participation of their children in the study and provided written informed consent.

Patient Selection

Sixteen patients were recruited from a school for children with physical disabilities (Institut Royal de l'Accueil du

Handicap Moteur, Brussels, Belgium). This sample size was dependent on the recruitment possibilities in the school. MG and AR enrolled the children. The patients' characteristics are described in Table 1. The inclusion criteria were a history of CP, a maximum age of 18 years, the ability to understand simple instructions, and moderate to severe impairments of the upper limbs, corresponding to a Manual Ability Classification System (MACS) score greater than 1. The exclusion criteria were epileptic patients and upper limb therapeutic intervention within the previous 6 months, such as a Botulinum toxin injection or neuro-orthopedic surgery. The patients were equally randomized into 2 groups (1:1): a Robotic group and a Control group. A stratified randomization assigned participants to their groups after the first evaluation using a computer-generated random number. The same persons (MG and AR) generated each allocation sequence. The stratification classified the subjects according to their upper limb manual capacity, as assessed by the MACS score (moderate disability, MACS range = 2-3; and severe disability, MACS range = 4-5). The trial was registered at ClinicalTrials.gov, number NCT01700153.

REAPlan

The robot used in this study was a robot research prototype named REAPlan, which is illustrated in Figure 1A.¹⁴ REAPlan is an end-effector robot that can move the patient's upper limb in a horizontal plane via a handle that the patient can grasp or to which he or she may be attached by an orthosis if his or her hand is too weak.

REAPlan is fitted with force and position sensors (acquisition frequency = 100 Hz), allowing for control of the lateral (\bar{F}_{lat}) and longitudinal (\bar{F}_{long}) interaction forces between the patient and the robot. Below, we provide the description of these 2 interaction forces (\bar{F}_{lat} and \bar{F}_{long}) and how these forces are automatically adapted in the function of the patient's performance.

The patient has to perform the movement along a reference trajectory. This reference trajectory corresponds to the ideal path that the patient must follow to perform the exercise. (\bar{F}_{lat}) corresponds to a lateral interaction force, perpendicular to the reference trajectory, that helps the patient stay on the path. The higher this interaction force, the more the robot is helping the patient stay on the reference trajectory. (\bar{F}_{long}) corresponds to a longitudinal interaction force, parallel to the reference trajectory, that helps the patient move along the trajectory at a reference speed. The higher this force, the more the robot helps the patient move along the reference trajectory at this reference speed. For this study, the reference speed was standardized at 5 cm/s. After reaching the end of a given trajectory (ie, the target), (\bar{F}_{long} and \bar{F}_{lat}) are automatically adapted in function of the patient's performance. If the patient reaches the target with a speed that is below the reference speed, (\bar{F}_{long}) increases to help the patient with respect to the reference speed, and

Table 1. Characteristics of the Subjects Included in the Robotic and Control Groups and Results of the Baseline Measurement Comparison Between the Groups and the Learning Effects of the Upper Limb Kinematics in All Children.

	Robotic Group, Mean (SD) (n = 8)	Control Group, Mean (SD) (n = 8)	P Value	Test 1, Mean (SD) (n = 16)	Test 2, Mean (SD) (n = 16)	Test 3, Mean (SD) (n = 16)	P Value
Characteristics							
Age, years, mean (SD)	10.8 (4.6)	11.0 (3.5)					
MACS (1-5), median [Q1-Q3]	3 [2-3.3]	2.5 [2-4]					
Quadri-/di-/hemiplegic, n	4/4/0	3/4/1					
Dominance, R/L, n	3/5	4/4					
Kinematic indices							
Amplitude (cm)	14.9 (7.2)	20.1 (5.0)	.12	17.5 (7.0)	17.8 (6.6)	17.1 (7.0)	.62
CV straightness (%)	6.9 (3.0)	3.7 (2.3)	.03 ^a	5.6 (3.7)	4.9 (3.5)	5.4 (5.0)	.83
Speed metric	0.42 (0.05)	0.46 (0.05)	.10	0.45 (0.05)	0.43 (0.07)	0.45 (0.06)	.25
CV jerk metric (%)	18.8 (2.8)	20.1 (2.7)	.36	19.5 (5.1)	20.1 (7.1)	16.4 (5.0)	.09
CV speed metric (%)	17.9 (4.1)	20.9 (7.9)	.39	18.7 (4.5)	19.1 (4.8)	20.5 (5.4)	.66
BB (blocks min ⁻¹)	13.0 (7.3)	13.4 (9.6)	.93				
QUEST (/100) ^b							
Dissociated mvts	37 [21.1-43.8]	44.8 [25-54.7]	.54				
Grasp	51.9 [18.5-72.5]	51.9 [25.9-75.0]	.80				
Weight bearing	45.5 [23.0-77.6]	74.0 [29.1-97.5]	.66				
Protective extension	0.0 [0.0-50.0]	41.7 [8.3-87.5]	.45				
Muscle torque (N m)							
Elbow flexion	9.9 (5.3)	11.7 (5.2)	.52				
Elbow extension	9.3 (4.0)	11.5 (5.8)	.40				
MAS (/5) ^b							
Shoulder adduction	0.5 [0.0-1.3]	0.0 [0.0-0.0]	.28				
Elbow flexion	2.0 [0.8-2.0]	1.0 [0.0-2.0]	.57				
Elbow extension	0.0 [0.0-0.3]	2.0 [0.0-2.0]	.13				
Elbow pronation	1.0 [0.0-2.0]	0.5 [0.0-2.0]	.78				
Wrist flexion	1.0 [0.8-2.0]	0.0 [0.0-0.5]	.20				
Finger flexion	0.0 [0.0-1.0]	0.0 [0.0-0.0]	.51				
Abilhand-Kids (logits)							
PEDI (/63) ^b	21 [20-30.5]	27 [18.5-46]	.90				
Life Habits (/248) ^b	106.5 [67.5-136.8]	148 [137-153.5]	.15				

Abbreviations: Q1, first quartile; Q3, third quartile; R, right; L, left; MACS, Manual Ability Classification System; BB, Box and Block test; MAS, Modified Ashworth Scale.

^aCorresponds to a significant baseline difference.

^bIndicates results with median [first quartile-third quartile].

vice versa. If the patient does not maintain the reference path when he moves toward the target, (\bar{F}_{lat}) increases to help the patient follow the path, and vice versa.

The size of the workspace was adapted to the child's morphology, within a square that was 0.8 m long on each side. Indeed, this workspace was as large as possible to stimulate the children, with regard to their arm lengths, to perform the largest movements with the robot. A screen and a speaker were installed in the robot to give visual and auditory feedback for performance.

Interventions

Both groups (Robotic and Control) received 5 sessions of therapy per week over the course of 8 weeks (40 sessions in all). Each session lasted 45 minutes. For the Control group, all the sessions were CT. The Robotic group received 2 RAT sessions and 3 CT sessions per week.

The children underwent their CT sessions with their regular physiotherapists and occupational therapists. The physiotherapists practiced neurodevelopmental therapy, and occupational therapists specifically focused on the ADL. The therapists maintained their standard protocols and adapted the rehabilitation to match each child's needs.

All RAT sessions were supervised by the same physiotherapist (MG), who is experienced with the use of robot. RAT sessions consisted of many duplicate exercises. Each exercise consisted of 160 consecutive movements toward a specific target, as suggested by Fasoli et al,⁸ with the REAPlan robotic device (for illustration, see Figure 1B). A force field helped the children reach the targets (see the REAPlan section). The reaching of each target consecutively resulted in audio feedback, the deletion of the target, and the appearance of a new target on the screen. This new target was randomly placed on the visual screen at a distance of 10 cm from the last one. These targets were enlarged

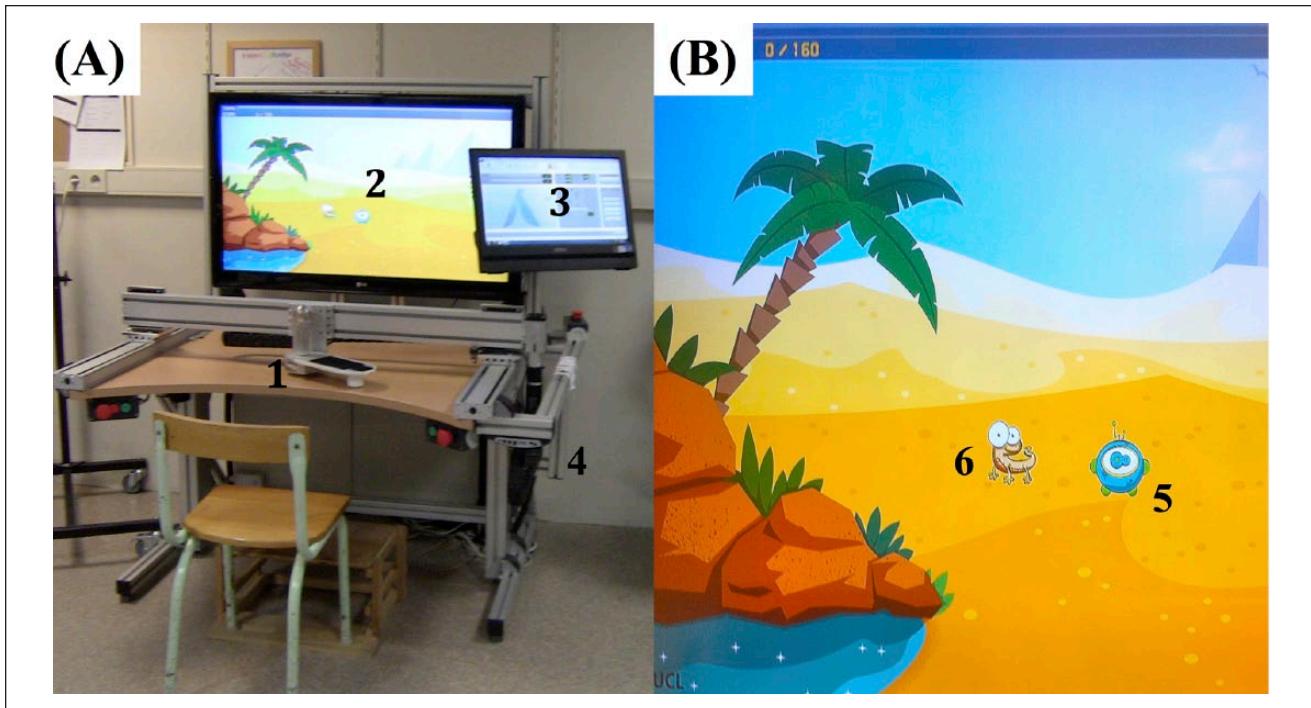


Figure 1. (A) View of REAPlan. (B) Zoomed-in view of the visual interface during a session of robotic-assisted therapy.
1 = Planar end-effector robot; 2 = Visual interface for the patient; 3 = Physiotherapist's interface; 4 = Adaptive button for the table height; 5 = Cursor to move; 6 = Target to reach.

for children with visual impairments. For half of the exercises, the target was motionless as long as the patient did not reach it. For the other half, the target was dynamic, moving a distance of 1 cm vertically or horizontally every 0.5 seconds.

The amount of movement, adapted to each patient, was as high as possible to stimulate improvements but was also adapted to the child's tiredness. Each child could have an optional rest between exercises and during each exercise (of approximately 1 minute). Finally, the RAT sessions were in the form of video games. An avatar (the cursor that the child had to move) and a cartoon animal (the target that the child had to reach) were integrated into an appropriate landscape (Figure 1B). The cartoon animal and its corresponding landscape were changed each week. Finally, at the end of each exercise, a personalized feedback was posted on the visual interface to congratulate the child and give him his time score for achieving the 160 targets.

ICF Assessment

All the children were assessed before and after the intervention through a protocol that took into account the 3 domains of the ICF.

The primary outcome was upper limb kinematics. Gilliaux et al^{18,19} provided a standardized protocol to quantitatively assess active movements of the upper limb in

stroke patients, including several kinematic indices. The short version of this protocol (5 indices) was used for this study. This protocol consisted of performing 4 different tasks (Free Amplitude, Target, Square, and Circle), as described below.

For the Free Amplitude task, the subject had to reach straight out in front of them as far as they could and brought the arm back to the starting position. For the Target task, the subject made movements in the most precise and direct manner toward a specific target placed at a distance of 10 cm in front of the subject. After performing this task, the robot brought the subject's arm back to the starting position. For the Square and Circle tasks, the subject had to draw 2 geometrical shapes: a square of 6 cm side and a circle of 4 cm radius. These shapes were performed clockwise with the right upper limb, and counterclockwise with the left one. These tasks were performed with REAPlan, without any assistance (ie, no interaction forces) and at spontaneous speeds.

For the Free Amplitude task, the computed indices were the amplitude and the coefficient of variation (CV) of the straightness. For the Target task, the speed metric index was calculated. For the Square and Circle tasks, the CV_{jerk metric} and CV_{speed metric} indices, respectively, were computed. Each index of this short protocol was computed for each of the 10 cycles of movement and was then averaged.

The kinematic assessment started after a 10-minute training phase to limit learning bias. For the acquisition phase, the order of tasks was randomly assigned. Each task was performed 10 consecutive times, during which the end-effector position was recorded (acquisition frequency = 100 Hz). The rest period between tasks was 1 minute. This kinematic assessment was performed 3 times within the 2 weeks preceding the intervention to evaluate a possible learning effect of the protocol and then once after the intervention. The same blinded physiotherapist (DD) performed each kinematic assessment.

For the secondary outcomes of the body structure and function domain of the ICF, the assessment included the Box and Block test (BB)²⁰; the 4 subscales (dissociated movements, grasps, weight bearing, and protective extension) of the Quality of Upper Extremity Skills Test (QUEST)^{21,22}; the Modified Ashworth Scale (6 muscular groups were tested: shoulder adductors, elbow flexors and extensors, pronators, wrist and finger flexors)²³; and the strength of 2 muscular groups (elbow flexors and extensors), assessed with a hand-held dynamometer (Microfet2TM, Orsay, France).²⁴ For the calculation of muscle torque, the result obtained with the dynamometer was multiplied by the distance measured between the lateral epicondyle and radial styloide.²⁵ All these assessment tools were reliable and valid for the studied population²⁶ and were used by the same blinded occupational therapist (DH).

The secondary outcomes of the activity and participation domains of the ICF correspond to 3 questionnaires. For the activity domain, the French versions of the Abilhand-Kids²⁷ and Pediatric Evaluation of Disability Inventory (PEDI)²⁸ questionnaires were filled out by each child's therapist. For the participation domain, the French version of Life Habits was completed by each child's parent.²⁹

Statistics

Statistical tests were performed using SigmaStat 3.5 software (WPCubed GmbH, Munich, Germany). For tests with parametric measures, the normal distribution and equality of variance were verified for all comparisons. For each test, the significance level was .05.

For each parametric and nonparametric measure, a 1-way analysis of variance (ANOVA) or a Mann-Whitney test was performed to verify the parity of the baseline results between groups. To verify the learning effect of the primary outcome, a 1-way repeated ANOVA was performed for each kinematic index on the 3 measures computed before the intervention.

For each parametric variable, a 2-way repeated ANOVA was performed to analyze the interaction between the time (before intervention vs after intervention) and groups (Control group vs Robotic group). For each significant interaction, a Bonferroni-adjusted post hoc (Holm Sidak)

test was used to analyze the differences in the change between groups. For each nonparametric variable, a Mann-Whitney test and a Wilcoxon test were performed to analyze the treatment effects between groups and within each group, respectively.

Results

The recruitment and baseline assessments were performed in September 2012, and the interventions were started in October 2012. The final interventions were completed in December 2012. The final assessments were performed between 1 and 7 days following the final rehabilitation session. The flowchart of this study is illustrated in Figure 2.

All 16 patients completed the study. During each RAT session, the patients performed 744 (224) (mean [SD]) movements on average with the REAPlan. For the Robotic group, the children performed 15 (0) sessions of RAT and 23 (0.9) sessions of CT. For the Control group, the children received 38.4 (1.7) sessions of CT. No adverse events were reported. All results are presented in Tables 1, 2, and 3 and are illustrated in Figure 3.

Similarity Between Groups at Baseline and Learning Effect

Before the interventions, the results of the kinematic indices were similar between groups, except for the CV_{straightness} of the Free Amplitude task ($P = .03$; Table 1). There was no learning effect for the primary outcome (Table 1). Indeed, for all merged tasks, the kinematic indices were similar within the 3 measures computed before the intervention ($P > .09$). For this reason, the average of these 3 kinematic measures was considered to be the baseline results.

Effect of Therapy

For the body structure and function domain, an interaction between the time and groups revealed that the smoothness in discrete and unidirectional upper limb movements only improved in children who received RAT ($P < .01$; Table 2). Indeed, for the Target task, the speed metric index increased from 0.42 (0.05) to 0.49 (0.03) in the Robotic group, but this index score did not change in the Control group (0.46 [0.05] to 0.46 [0.06]). For the 3 other tasks (Free Amplitude, Square, and Circle), the kinematics indices did not change after intervention ($P > .05$).

An interaction between time and groups showed that the manual dexterity of the upper limb improved significantly more in children who received RAT than children who only received CT ($P = .04$; Table 2). Indeed, the BB score improved from 13.0 (7.3) to 16.6 (9.9) blocks/min in the Robotic group, while this score increased only slightly from 13.4 (9.6) to 13.8 (9.7) in the Control group.

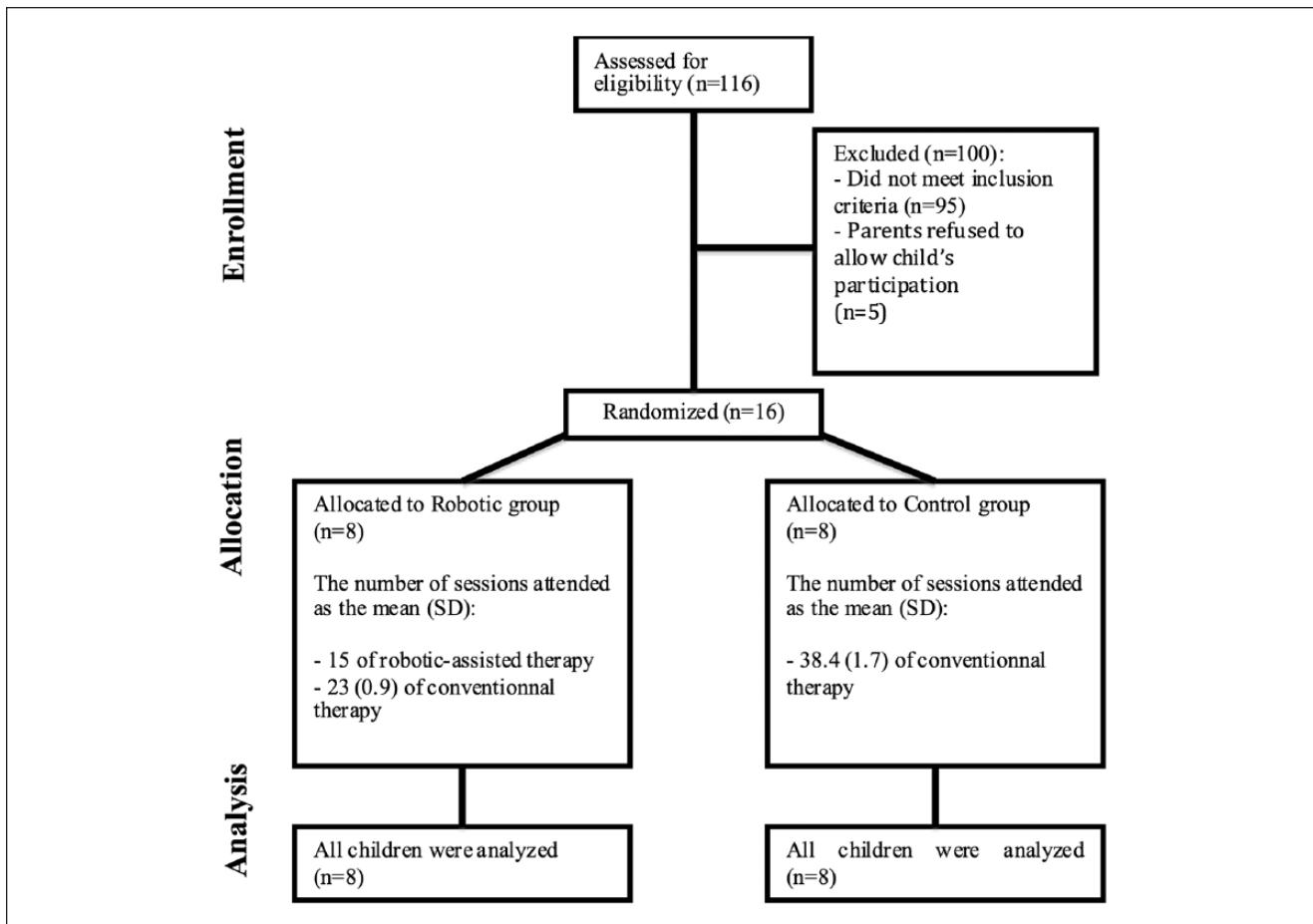


Figure 2. Flow diagram of the participants through each stage of the study (ie, Enrollment, Allocation, and Analysis). Adapted from CONSORT (Moher et al³⁸).

The capacity to perform analytical movements of the upper limb similarly improved in both groups ($P < .05$; Table 3). Indeed, the scores of the dissociated movements subscale of the QUEST significantly increased for the Robotic (median increased from 37.0 to 63.3/100) and Control (median increased from 44.4 to 68.8) groups ($P < .04$). However, these improvements were not different between the groups ($P = .87$; Table 3).

There was no significant effect of treatment for the other scales and for the 3 questionnaires assessing the activity and participation domains ($P > .06$; Tables 2 and 3).

Discussion

The aim of this study was to compare the effect of conventional therapy (CT) to the combination of RAT and CT in children with CP in a single-blind randomized controlled protocol. This comparison took into account the 3 domains of the ICF.³⁰

Body Structure and Function Domain

Some upper limb kinematic indices, assessed by the robot REAPlan, and manual dexterity, assessed by the Box and Block test, had significantly more improvement after RAT and CT than after CT alone. Both results suggest a motor learning effect.⁷ Indeed, the RAT of this study consisted of repetitive discrete movements (reaching targets), and the observed improvements were specifically related to discrete movements (Target Task of the kinematic assessment and BB).

The assessment protocol of this study followed current recommendations. Indeed, kinematics was chosen as a primary outcome to quantitatively and objectively assess upper limb movements,³¹ avoiding the disadvantages (eg, nonparametrical statistics) of qualitative, subjective, and ordinal scales.^{31,32} After that, this protocol was established to be easily reproduced in clinical routines. Because a robotic device, such as the REAPlan, has the potential to

Table 2. Two-Way ANOVA Results for Parametric Variables Comparing the Treatment Effects Between the Robotic and Control Groups.

	T1-T0, Mean Difference (SD)		Group Effect, P Value	Time Effect, P Value	Interaction: Group × Time Effect, P Value	Effect Size, Cohen's <i>d</i>				
	Robotic Group (n = 8)	Control Group (n = 8)								
Kinematic indices										
Free amplitude										
Amplitude (cm)	1.7 (1.6)	0.6 (3.1)	.15	.37	.08	0.48				
CV _{straightness} (%)	0.8 (6.4)	1.1 (2.5)	.05	.92	.45	-0.06				
Target										
Speed metric	0.07(0.05)	0.00 (0.05)	.75	<.01*	.01*	1.52				
Square										
CV _{jerk metric} (%)	-0.8 (6.5)	0.4 (8.2)	.49	.50	.50	-0.17				
Circle										
CV _{speed metric} (%)	2.5 (6.8)	0.0 (7.1)	.26	.75	.92	0.36				
BB (blocks min ⁻¹)	3.6 (3.6)	0.4 (2.1)	.79	.04*	.02*	1.14				
Muscle torques (N m)										
Elbow flexion	1.5 (4.9)	2.9 (3.3)	.59	.53	.07	-0.34				
Elbow extension	0.6 (2.5)	2.1 (3.1)	.45	.31	.09	-0.54				
Abilhand-Kids (logits)	-0.2 (0.8)	-1.1 (1.3)	.71	.15	.06	0.93				

Abbreviations: CV, coefficient of variation; BB, Box and Block test.

*Effect size was rated as large, medium, and small with Cohen's *d* scores >0.8, 0.5 to 0.8, and <0.5, respectively.*Indicates significant results (*P* < .05).**Table 3.** Results of the Mann-Whitney and Wilcoxon Tests for Nonparametric Variables Comparing the Treatment Effects Between the Robotic and Control Groups and Within Each Group.

	Mann-Whitney Test			Wilcoxon Test		
	Robotic Group (n = 8)	Control Group (n = 8)		Robotic Group (n = 8)		Control Group (n = 8)
				T1-T0		T1
QUEST (/100)						
Dissociated movements	23.5 [5.7; 41.0]	28.1 [21.9; 36.4]	37.0 [21.1; 43.8]	63.3 [41.3; 74.3]*	44.4 [25; 54.7]	68.8 [44.9; 83.3]*
Grasp	9.3 [-9.5; 23.1]	12.7 [1.9; 23.2]	51.9 [18.5; 72.5]	59.3 [41.7; 85.2]	51.9 [25.9; 75.0]	55.6 [39.8; 75.8]
Weight bearing	10.3 [3.0; 24.5]	0.0 [-9.0; 0.0]	45.5 [23.0; 77.6]	65.0 [30.0; 88.0]	74.0 [29.1; 97.5]	71.0 [16.0; 94.5]
Protective extension	0.0 [0.0; 19.5]	0.0 [0.0; 2.1]	0.0 [0.0; 50.0]	27.8 [12.5; 100]	41.7 [8.3; 87.5]	52.8 [9.0; 92.4]
MAS (/5)						
Shoulder adduction	0.0 [-0.3; 0.0]	0.0 [0.0; 0.0]	1.0 [0.0; 1.3]	0.0 [0.0; 1.3]	0.0 [0.0; 0.0]	0.0 [0.0; 0.0]
Elbow flexion	0.0 [-0.3; 0.0]	0.0 [0.0; 0.0]	2.0 [0.8; 2.0]	1.5 [0.0; 2.0]	0.5 [0.0; 2.0]	1.0 [0.0; 2.0]
Elbow extension	0.0 [0; 0.3]	0.0 [0.0; 0.5]	0.0 [0.0; 0.3]	0.0 [0.0; 2.0]	2.0 [0.0; 2.0]	2.0 [1.8; 2.0]
Elbow pronation	0.0 [-1.0; 0.0]	0.0 [-0.3; 0.0]	1.5 [0.0; 2.0]	1.0 [0.0; 2.0]	0.5 [0.0; 2.0]	0.0 [0.0; 0.5]
Wrist flexion	0.0 [-1.0; 0.0]	0.0 [0.0; 0.0]	1.0 [0.8; 2.0]	0.5 [0.0; 1.3]	0.0 [0.0; 2.0]	0.0 [0.0; 2.0]
Finger flexion	0.0 [0.0; 0.0]	0.0 [0.0; 0.0]	0.0 [0.0; 1.3]	0.5 [0.0; 1.0]	0.0 [0.0; 0.5]	0.0 [0.0; 0.0]
PEDI (/126)	0.0 [-1.5; 2]	2.0 [-2.5; 3.5]	21.0 [20.0; 39.5]	24.0 [20.3; 32.3]	27.0 [18.5; 46.0]	42.5 [18.0; 48.5]
Life-Habits (/248)	8.5 [-6.3; 30.0]	12.0 [-9.0; 21.0]	106.5 [67.5; 136.8]	113.5 [101.3; 135.5]	148.0 [137.0; 153.5]	154.0 [139.0; 163.0]

Abbreviations: QUEST, Quality of Upper Extremity Skills Test; MAS, Modified Ashworth Scale; PEDI, Pediatric Evaluation of Disability Inventory.

The values are presented as medians [first quartiles; third quartiles]. T0 and T1 correspond to the results before and after the intervention, respectively. T1-T0 corresponds to the difference between the results obtained after (T1) and before (T0) the intervention.

*Indicates a significant difference (*P* < .05).

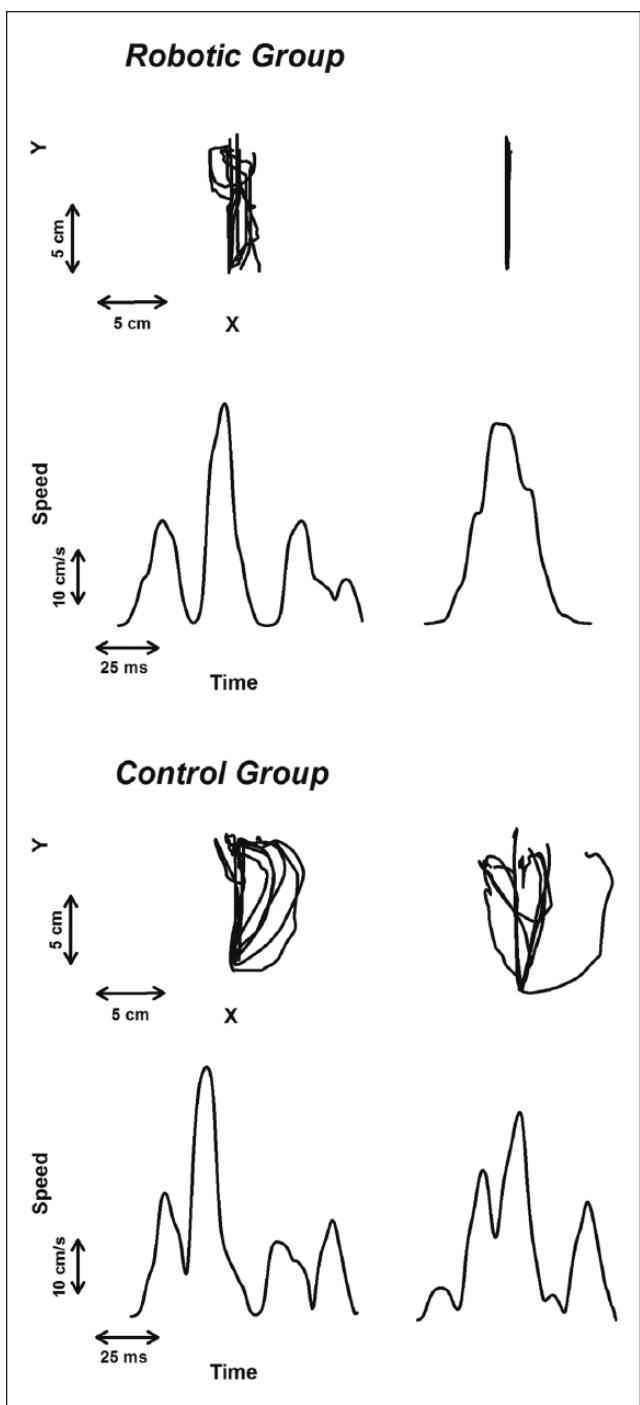


Figure 3. For the target task in each group (Robotic and Control), illustration of the typical traces computed for one child before (left graphs) and after (right graphs) treatment. The upper graphs show the displacement plots of 10 consecutive trials. The lower graphs show the speed curve of one in-progress trial.

rehabilitate and assess patients,¹⁹ we suggest that combining both abilities in one tool is more advantageous in clinical routines than adding other kinematic assessment tools, such as an expensive optoelectronic system.

However, one can argue that the kinematic improvement observed in the Robotic group could be related to the child's learning of the specific robot tasks. Even so, the 3 kinematic assessments performed before the intervention did not show any leaning effect. More important, the Robotic group transferred the improvement to a more functional task (BB) that was not directly related to robot therapy. Indeed, improvement in the BB test showed a high effect size (Cohen's $d = 1.1$), which suggests that RAT can significantly influence gross manual ability in children. However, although minimal detectable change in CP is unknown, the change measured (3.6 blocks/min) is below the known minimum for stroke patients (6 block/min)³³ and cannot therefore be assumed to represent a meaningful improvement. These results are consistent with an observational study that has shown kinematic improvements after RAT in children with CP.³⁴ Finally, randomized controlled trials assessing RAT efficacy in stroke patients have also shown improvements in kinematics and manual dexterity, as assessed by a robot^{35,36} and the BB,³⁷ respectively.

The dissociated movements of the QUEST showed improvements in both groups, but no difference between groups. Previous observational studies identified significant improvements on this same subscale after RAT.^{8,34} The present results illustrate the necessity of a control group in clinical trials to avoid misinterpretation of the results.³⁸ The improvement observed in both groups could be explained by the fact that this study started after the summer holidays (lasting 2 months), during which most children did not have rehabilitation. This observation suggests that CT, with or without RAT, could preserve the children's capacity to dissociate upper limb movements.

Activity and Participation Domains

The improvements of impairments after only 8 weeks of RAT seem promising. However, these improvements did not translate into improved ADL. This result is disappointing because the patients yearn to improve their capacity for ADL as well as their social integration. These results can be explained by the following hypotheses. First, the various exercises were designed to stimulate the patients to repeat discrete reaching movements. However, ADL involves discrete reaching movements (eg, pushing on a light switch) along with rhythmic reaching movements (eg, washing the upper body) and grasping movements (eg, open a bag chips) (for these examples, see Abilhand-Kids²⁷). Further studies should expand the exercises to enable the patients to repeat a wide variety of movements (eg, rhythmic, discrete, with or without hand implication), as suggested by Krebs et al.³⁴ Moreover, these exercises could be in the form of ADL¹⁰ or serious games.³⁹ Second, the activity and participation assessments were presented in the form of questionnaires completed by parents and therapists.²⁷⁻²⁹ Because the

parents and therapists were not blinded, their judgment could have been altered. To increase the responsiveness of this activity assessment, future studies should also use tools to assess the child's performance in ADL, such as the Melbourne Assessment of Unilateral Upper Limb Function⁴⁰ or the Assisting Hand Assessment.⁴¹

Limitations and Perspectives

This study lays the groundwork for future research on the use of RAT in CP.

Even though the sample size was sufficient to show significant results, it was too small to generalize the results to the clinical setting and to determine the subgroups of children who will be more responsive to RAT. Finally, the sample size did not allow the stratification to take other factors, such as the patients' ages, into account. This bias was limited because the mean age of each group was similar (Table 1). Then, further multicenter trials should be planned to (a) confirm these results with a larger sample and variety of settings³⁸; (b) add other stratification factors, such as the patients' age, since learning capacities and video games playing experience are not the same among young children and adolescents; and (c) establish the correlations between the improvements and the children's characteristics (eg, impairment severity, age, etc).

In this study, the proportion of robotic sessions (2/5) was limited by the feasibility of performing the study at school, and the number of RAT sessions ($n = 15$) was chosen in agreement with previous studies.^{8,11,13} However, we still do not know whether more intensive use of the robot or the use of RAT over a longer period of time would yield better results. Additionally, we do not know whether similar results could be obtained with reduced use of the robot. This issue could be addressed through a study conducted over a longer period of time with a regular evaluation of the evolution of the patients' function instead of only at the beginning and after therapy.

This study assessed the effect of RAT directly after therapy but not a few months later for logistical reasons. There was no long-term follow-up; therefore, the results do not provide any indication that benefits are maintained or of the necessity to repeat RAT regularly or to use it continuously. This limitation could be addressed by evaluating the evolution of improvements over time, as Krebs et al³⁴ have shown for kinematics.

Finally, Sakzewski et al⁵ are interested in combining botulinum toxin with other upper limb therapies. Future studies should evaluate the effectiveness of the combination of RAT with botulinum toxin injection in the upper limb. This combination showed promising results in a pilot study and could maximize the improvements to upper limb impairments and activities after RAT.⁴²

Conclusions

In conclusion, this study is the first single-blind randomized controlled trial to assess the efficacy of RAT in children with CP. This therapy improved upper limb kinematics and manual dexterity but did not improve functional activities and social participation. Further studies should confirm these preliminary results on larger populations and assess if RAT could lead to more functional improvements in the long term. The REAPlan robotic device provides an intensive, goal-oriented, and assist-as-needed therapy associated with motivational and performance feedbacks. Robotic devices offer children fun and intensive rehabilitation that a human therapist cannot provide. These robots can be easily integrated as a relevant complement to therapy in the clinical setting.

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References

1. Blair E, Watson L. Epidemiology of cerebral palsy. *Semin Fetal Neonatal Med.* 2006;11:117-125.
2. Cans C, De-la-Cruz J, Mermet MA. Epidemiology of cerebral palsy. *Paediatr Child Health.* 2008;18:393-398.
3. Eunson P. Aetiology and epidemiology of cerebral palsy. *Paediatr Child Health.* 2012;22:361-366.
4. Aisen ML, Kerkovich D, Mast J, et al. Cerebral palsy: clinical care and neurological rehabilitation. *Lancet Neurol.* 2011;10:844-852.
5. Sakzewski L, Ziviani J, Boyd R. Systematic review and meta-analysis of therapeutic management of upper-limb dysfunction in children with congenital hemiplegia. *Pediatrics.* 2009;123:1111-1122.
6. Holt RL, Mikati MA. Care for child development: basic science rationale and effects of interventions. *Pediatr Neurol.* 2011;44:239-253.
7. Garvey MA, Giannetti ML, Alter KE, Lum PS. Cerebral palsy: new approaches to therapy. *Curr Neurol Neurosci Rep.* 2007;7:147-155.

8. Fasoli SE, Fragala-Pinkham M, Hughes R, Hogan N, Krebs HI, Stein J. Upper limb robotic therapy for children with hemiplegia. *Am J Phys Med Rehabil.* 2008;87:929-936.
9. Fasoli SE, Ladenheim B, Mast J, Krebs HI. New horizons for robot-assisted therapy in pediatrics. *Am J Phys Med Rehabil.* 2012;91:280-289.
10. Fluet GG, Qiu Q, Kelly D, et al. Interfacing a haptic robotic system with complex virtual environments to treat impaired upper extremity motor function in children with cerebral palsy. *Dev Neurorehabil.* 2010;13:335-345.
11. Frascarelli F, Masia L, Di Rosa G, et al. The impact of robotic rehabilitation in children with acquired or congenital movement disorders. *Eur J Phys Rehabil Med.* 2009;45:135-141.
12. Pignolo L. Robotics in neuro-rehabilitation. *J Rehabil Med.* 2009;41:955-960.
13. Krebs HI, Palazzolo JJ, Dipietro L. Rehabilitation robotics: performance-based progressive robot-assisted therapy. *Auton Robot.* 2003;15:7-20.
14. Sapin J. Conception d'un robot interactif pour la re-education des membres supérieurs de patients cérébrolésés [PhD thesis]. Louvain-la-Neuve, Belgium: Université catholique de Louvain; 2010.
15. Mehrholz J, Hädrich A, Platz T, Kugler J, Pohl M. Electromechanical and robot-assisted arm training for improving generic activities of daily living, arm function, and arm muscle strength after stroke. *Cochrane Database Syst Rev.* 2012;(6):CD006876.
16. Aharonson V, Krebs HI. Prediction of response to robot-aided motor neuro-rehabilitation of children with cerebral palsy. *Biomed Signal Process Control.* 2012;7:180-184.
17. Krebs HI, Ladenheim B, Hippolyte C, Monterroso L, Mast J. Robot-assisted task-specific training in cerebral palsy. *Dev Med Child Neurol.* 2009;51:140-145.
18. Gilliaux M, Lejeune T, Detrembleur C, Sapin J, Dehez B, Stoquart G. A robotic device as a sensitive quantitative tool to assess upper limb impairments in stroke patients: a preliminary prospective cohort study. *J Rehabil Med.* 2012;44:210-217.
19. Gilliaux M, Lejeune T, Detrembleur C, et al. Using the robotic device REAplan as a valid, reliable, and sensitive tool to quantify upper limb impairments in stroke patients. *J Rehabil Med.* 2014;46:117-125.
20. Mathiowetz V, Volland G, Kashman N, Weber K. Adult norms for the Box and Block Test of manual dexterity. *Am J Occup Ther.* 1985;39:386-391.
21. DeMatteo C, Law M, Russell D, Pollock N, Rosenbaum P, Walter S. *QUEST: Quality of Upper Extremity Skills Test.* Hamilton, Ontario, Canada: McMaster University, Neurodevelopmental Clinical Research Unit; 1992.
22. Thorley M, Lannin N, Cusick A, Novak I, Boyd R. Reliability of the quality of upper extremity skills test for children with cerebral palsy aged 2 to 12 years. *Phys Occup Ther Pediatr.* 2012;32:4-21.
23. Numanoğlu A, Günel MK. Intraobserver reliability of modified Ashworth scale and modified Tardieu scale in the assessment of spasticity in children with cerebral palsy. *Acta Orthop Traumatol Turc.* 2012;46:196-200.
24. Willemse L, Brehm MA, Scholtes VA, Jansen L, Woudenberg-Vos H, Dallmeijer AJ. Reliability of isometric lower-extremity muscle strength measurements in children with cerebral palsy: implications for measurement design. *Phys Ther.* 2013;93:935-941.
25. Eek MN, Kroksmark AK, Beckung E. Isometric muscle torque in children 5 to 15 years of age: normative data. *Arch Phys Med Rehabil.* 2006;87:1091-1099.
26. Wagner LV, Davids JR. Assessment tools and classification systems used for the upper extremity in children with cerebral palsy. *Clin Orthop Relat Res.* 2012;470:1257-1271.
27. Arnould C, Penta M, Renders A, Thonnard JL. ABILHAND-Kids: a measure of manual ability in children with cerebral palsy. *Neurology.* 2004;63:1045-1052.
28. Berg M, Jahnsen R, Frøslie KF, Hussain A. Reliability of the Pediatric Evaluation of Disability Inventory (PEDI). *Phys Occup Ther Pediatr.* 2004;24:61-77.
29. Noreau L, Lepage C, Boissiere L, et al. Measuring participation in children with disabilities using the Assessment of Life Habits. *Dev Med Child Neurol.* 2007;49:666-671.
30. Gutenbrunner C, Meyer T, Melvin J, Stucki G. Towards a conceptual description of physical and rehabilitation medicine. *J Rehabil Med.* 2011;43:760-764.
31. Balasubramanian S, Colombo R, Sterpi I, Sanguineti V, Burdet E. Robotic assessment of upper limb motor function after stroke. *Am J Phys Med Rehabil.* 2012;91:255-269.
32. Sivan M, O'Connor R, Makower S, Levesley M, Bhakta B. Systematic review of the outcome measures used in the evaluation of robot-assisted upper limb exercise in stroke. *J Rehabil Med.* 2011;43:181-189.
33. Chen HM, Chen CC, Hsueh IP, Huang SL, Hsieh CL. Test-retest reproducibility and smallest real difference of 5 hand function tests in patients with stroke. *Neurorehabil Neural Repair.* 2009;23:435-440.
34. Krebs HI, Fasoli SE, Dipietro L, et al. Motor learning characterizes habilitation of children with hemiplegic cerebral palsy. *Neurorehabil Neural Repair.* 2012;26:855-860.
35. Daly JJ, Hogan N, Perepezko EM, et al. Response to upper-limb robotics and functional neuromuscular stimulation following stroke. *J Rehabil Res Dev.* 2005;42:723-736.
36. Fasoli SE, Krebs HI, Stein J, Frontera WR, Hogan N. Effects of robotic therapy on motor impairment and recovery in chronic stroke. *Arch Phys Med Rehabil.* 2003;84:477-482.
37. Bovolenta F, Goldoni M, Clerici P, Agosti M, Franceschini M. Robot therapy for functional recovery of the upper limbs: a pilot study on patients after stroke. *J Rehabil Med.* 2009;41:971-975.
38. Moher D, Hopewell S, Schulz KF. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *J Clin Epidemiol.* 2010;63:1-37.
39. Wolinsky FD, Vander Weg MW, Howren MB, Jones MP, Dotson MM. A randomized controlled trial of cognitive training using a visual speed of processing intervention in middle aged and older adults. *PLoS One.* 2013;8:e61624.
40. Randall M, Carlin JB, Chondros P, Reddiough D. Reliability of the Melbourne assessment of unilateral upper limb function. *Dev Med Child Neurol.* 2001;43:761-767.
41. Holmefur M, Aarts P, Hoare B, Kruimlinde-Sundholm L. Test-retest and alternate forms reliability of the assisting hand assessment. *J Rehabil Med.* 2009;41:886-891.
42. Fasoli SE, Fragala-Pinkham M, Hughes R, Krebs HI, Hogan N, Stein J. Robotic therapy and botulinum toxin type A: a novel intervention approach for cerebral palsy. *Am J Phys Med Rehabil.* 2008;87:1022-1025.