BMJ Open

Effectiveness of robotic-assisted therapy for upper extremity function in children and adolescents with cerebral palsy: a systematic review protocol

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To cite: Sung-U S, Nisa BU, Yotsumoto K, *et al*. Effectiveness of robotic-assisted therapy for upper extremity function in children and adolescents with cerebral palsy: a systematic review protocol. *BMJ Open* 2021;**11**:e045051. doi:10.1136/bmjopen-2020-045051

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2020-045051).

Received 21 September 2020
Revised 15 December 2020
Accepted 16 April 2021

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ABSTRACT

Introduction The application of advanced technologies in paediatric rehabilitation to improve performance and enhance everyday functioning shows considerable promise. The aims of this systematic review are to investigate the effectiveness of robotic-assisted therapy for upper extremity function in children and adolescents with cerebral palsy and to extend the scope of intervention from empirical evidence.

Methods and analysis Multiple databases, including MEDLINE (Ovid), PubMed, CINAHL, Scopus, Web of Science, Cochrane Library and IEEE Xplore, will be comprehensively searched for relevant randomised controlled trials and non-randomised studies. The grey literature will be accessed on the ProQuest Dissertations & Theses Global database, and a hand search from reference lists of previous articles will be performed. The papers written in English language will be considered, with no limitation on publication date. Two independent reviewers will identify eligible studies, evaluate the level of evidence (the Oxford Centre for Evidence-Based Medicine) and appraise methodological quality and risk of bias (the Standard quality assessment criteria for evaluating primary research papers from a variety of fields (QualSyst tool); the Grading of Recommendations Assessment, Development and Evaluation). Data will be appropriately extracted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guideline. A narrative synthesis will be provided to summarise the results, and a meta-analysis will be conducted if there is sufficient homogeneity across outcomes.

PROSPERO registration number CRD42020205818.

Ethics and dissemination Ethical approval is not required for this study. The findings will be disseminated via a peer-reviewed journal and international conferences.

Strengths and limitations of this study

- This systematic review protocol focuses specifically on the evidence of the effectiveness and the suitability of service delivery through robotic-assisted therapy for upper extremity function in children and adolescents with cerebral palsy.
- Intervention outcomes will be described and classified according to the International Classification of Functioning, Disability and Health, version for Children and Youth.
- We anticipate that meta-analysis could be challenging due to the methodological heterogeneity of feasibility studies.

INTRODUCTION

With a prevalence of approximately 2–3 per 1000 livebirths,[1 2] cerebral palsy (CP) is one of the most common physical and developmental disabilities in childhood. CP is caused by a non-progressive lesion in the developing brain during the prenatal, perinatal or postnatal periods, and presents lifelong and heterogeneous neurological conditions.[1 3] An acknowledge consensus definition from 2006, describes CP as 'a group of permanent disorders of the development of movement and posture, causing activity limitation'.[4]

Early signs of CP usually emerge before the first or second year of life, when infants fail to reach key milestones at the expected age.[1 5] Through childhood, the clinical features of neuromotor impairments become more remarkable and variable in types and severity. The manifestations of CP chiefly include abnormalities of muscle tone and reflexes, impaired selective motor control, lack of coordination, atypical posture and movement patterns and delayed gross and fine motor development. In addition, CP is often accompanied by comorbidities and secondary problems, such as visual and hearing deficits, intellectual disabilities, epilepsy, contracture and deformities.[1 4 6 7]

Besides symptoms, CP can be displayed within the International Classification of Functioning, Disability and Health (ICF) and the derived version for Children and Youth (ICF-CY) (WHO).[8 9] Several studies have reported that children and adolescents with CP exhibit

various impairments in body function and structure, and have difficulties performing a wide range of activities.[10 11] The limitations in everyday functioning are common in mobility, self-care,[10 12 13] play,[14 15] school[16 17] and physical activities.[18 19] Moreover, children and adolescents with CP engage poorly in social and leisure activities comparing to normally developing peers.[20 21] These limitations and restrictions interrelate to a number of contextual factors, which may facilitate or hinder individuals with CP to be more or less independent living and health outcomes.[22 23]

The management of CP requires a multidisciplinary, holistic and long-term care approaches, involving medical and pharmacological treatments, rehabilitation interventions and assistive technologies alongside complementary and alternative remedies.[24 25] In the 21st century, advanced rehabilitation technologies are more available to patients with neurological conditions, in particular therapeutic robots.[26] Robotic devices have been widely integrated into clinicians' service in order to mediate and assist interventions to enhance clients' recovery and clinical outcomes resulting from stroke, traumatic brain injury, multiple sclerosis, spinal cord injury and other congenital and acquired movement disorders.[26–28]

There is a growing need of robotic-assisted therapy in the paediatric field and care delivery for children and adolescents with CP.[29 30] Based on the applying principles of neural plasticity, motor control and motor learning, robotic rehabilitation premises in the adaptability of the brain, which may occur spontaneously over time and/or be induced by movement practice after lesion.[31–33] Thus, the implementation of robotics primarily focuses on functional motor performance by providing intensive repetitive training, sensorimotor integration and cognitive engagement through goal-directed tasks to address the underlying symptoms and related problems due to client's neurological conditions.[34–36] From previous studies, the use of robotic devices has been found to improve kinematics,[37–40] range of motion,[41 42] muscle tone,[43 44] postural control[45 46] and functionality of upper[38 40] and lower extremities[47 48] among individuals with CP.

For upper extremity motor performance, there is evidence that up to 80% of CP clients have upper limb involvement and demonstrate limited functions.[49] In general, the acquisition of efficient arm and hand skills for use in daily life is a complex process that not only requires neuromusculoskeletal integrity, but also involves various aspects of a child's capabilities. Therefore, apart from positive symptoms that typically present patterns of spasticity, children and adolescents with CP often have a poor ability to reach, grasp, release and manipulate objects. Furthermore, they experience difficulty using their upper extremities to perform self-care and other activities.[50–52] These problems present great challenges in management and provision of therapeutic intervention, and even in the development and application of innovative technologies such as robotic devices.

To date, varying interventions are recommended to ameliorate movements and activities in upper extremity for CP clients, for example constraint-induced movement therapy, hand-arm bimanual intensive therapy, neurodevelopmental therapy, intramuscular injection of botulinum neurotoxin A, as well as, robotic-assisted therapy.[36 53–55] Current robotic devices for upper extremity rehabilitation are founded on two main designs. First, an end-effector is a robotic device in which movements are generated from the contact point in the most distal part of the extremity. Second, as a wearable robotic device, an exoskeleton attaches to multiple joints that can reproduce movements in the corresponding parts of the extremity at the same time.[56 57] Both robotic types have been applied to individuals diagnosed with CP and robots now can be used in combination with virtual and augmented reality during training. This could encourage a child's attention and motivation, and may contribute to better performance.[34 58]

Although the use of robots to improve functioning of upper extremities shows promise, the level of evidence in the paediatric group appears less than in adults. Most of robotic studies in children and adolescents with CP have relatively small sample size and few randomised controlled trials (RCTs).[30 58] Thus, its effectiveness among this client group is needed to prove clinically. In the past 5 years, the authors have found three literature reviews focusing on robotic devices for upper extremity function of individuals with CP, but only one has examined the effect size from studies offering sufficient data. The results have shown that robotic-assisted therapy had a moderate effect on reaching duration, smoothness and muscle tone, and a small to large effect on standardised clinical assessment.[59]

In another systematic research, a prior study has critically reviewed robotic-assisted therapy for locomotion and manipulation in children with CP. The results also indicated a limited number of robotic systems targeting upper extremity function.[60] In an earlier study, the researchers have comprehensively focussed on robotic devices and protocols for upper extremity function in children with neuromotor disorders.[61] Summaries of these reviews laid understanding of the control schemes and state of the art in the implementation of rehabilitation robots, particularly for children who have upper extremity impairments. However, the extent of service in the perspective of clinical intervention still requires a broader scope to assemble knowledge on robotic-assisted therapy and provide explicit information on complementary and alternative approaches for upper extremity function in people with CP.

To fill the research gaps, the present systematic review of robotic-assisted therapy for upper extremity function may help to verify if this approach is worthwhile for children and adolescents with CP, and how it may be best delivered. In addition, since some recently published studies have reported the beneficial effects of robotic rehabilitation on day-to-day activities, the outcomes will be described and classified into (1) body function and structure and (2) activity and participation, following the ICF-CY framework.

OBJECTIVES

The objectives of this study are:

1. To investigate the effectiveness of robotic-assisted therapy for upper extremity function in children and adolescents with CP on the outcomes within the domains of the ICF-CY.
2. To gain insight into the intervention of robotic-assisted therapy for upper extremity function in children and adolescents with CP.

METHOD

Study design

This protocol was developed in accordance with the recommendation of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P)[62] and the guideline of the PRISMA statement.[63 64]

Eligibility criteria

Studies will be considered following the population, intervention, comparator, outcomes and study designs approach.[64]

Participants

We will include the studies involving children and/or adolescents diagnosed with CP in the age range between 0 and 18 years. There are no limitations on gender, types (eg, spastic hemiplegia/diplegia/quadriplegia, dyskinetic, ataxic or mixed types) and severity of CP (eg, mild/moderate/severe CP; levels of gross motor/manual ability/communication functions).

Intervention

Robotic is defined as 'the application of electronic, computerised control systems to mechanical devices designed to perform human function'.[65] In the present systematic review protocol, robotic-assisted therapy refers to the incorporation of robotic devices targeting the entire or the specific parts of upper extremity into therapeutic training sessions for children and/or adolescents with CP. Studies will be considered either focussed on robotic rehabilitation alone or integrated with other approaches, tasks or technologies (eg, play, games or virtual reality). There are no limitations on settings (eg, clinical-based, school-based or home-based settings) and healthcare professionals who provide services (eg, occupational therapist, physiotherapist or rehabilitation nurse).

Comparator

Robotic-assisted therapy should be compared with a control intervention, trails with different arms or experiments with different conditions (eg, no treatment, placebo or treatment as usual).

Outcomes

All changes in the scores of outcome measures with at least two times of assessment (eg, baseline or pretest and posttest or follow-up) will be explored for the effect size and the effectiveness of robotic-assisted intervention. These functioning outcomes will be categorised according to the components and domains of the ICF-CY framework,[9 66–68] as follows:

1. Body function and structure will encompass the measures of functioning at the level of the body systems or body parts, particularly neuromusculoskeletal and movement-related functions of upper extremity. For example, the range of motion test, the manual muscle test, the Ashworth Scale or Modified Ashworth Scale, the Fugl-Meyer Assessment for Upper Extremity and the three-dimensional motion analysis.
2. Activity and participation will comprise the measures of functioning at the level of an individual in performing tasks or actions and in involving life situations. The domains of outcomes will focus especially on the ability to grasp, release and manipulate objects and ability to use upper extremity for self-care and other day-to-day activities. For instance, the ABILHAND-Kids, the Assisting Hand Assessment, the Melbourne Assessment of Upper Limb Function, the Functional Independence Measure for Children and the Children's Assessment of Participation and Enjoyment.

Study types

We will include all RCTs (eg, parallel, cluster and crossover designs) and non-randomised studies (NRSs) (eg, cohort, case–control and case series studies). We will exclude case reports, qualitative studies and secondary research (eg, review, systematic review and meta-analysis).

Search strategy

The relevant articles with English full text will be conducted from electronic databases, including MEDLINE (Ovid), PubMed, CINAHL, Scopus, Web of Science, Cochrane Library and IEEE Xplore for identification of evidence without date of publication restrictions. The search terms will be initially developed following the search strategy of MEDLINE by combining medical subject headings, free text words and Boolean operators in titles, abstracts and keywords (table 1). These terms and strategy will be appropriately modified for other databases. The grey literature will also be accessed on the ProQuest Dissertations & Theses Global database, and a hand search from reference lists of previous papers will be performed. However, the related systematic reviews will be used to facilitate searching of primary sources, but will not include in the final evidence.

Study selection

Initially, database searching and removing duplicate papers will be processed by one reviewer (SS-U). In the second step, two reviewers (SS-U, BUN) will independently screen titles and abstracts of the remaining articles to select potentially relevant studies that meet the inclusion and exclusion criteria. In the last step, independent reviewers will read the full texts of selected papers to verify their suitability for final review. Any possible disagreement between two reviewers

Table 1 Search strategy Medline (Ovid)

#	Search
1	cerebral palsy/
2	(hemipleg* or hemipare* or dipleg* or dipare* or quadripleg* or quadripare* or dyskine* or atheto* or dystoni* or chorea* or ataxi*).mp.
3	child/ or adolescent/
4	(child* or preschool or adolescen* or youth or teen* or student* or pediatric*).mp.
5	robot*.mp.
6	(end effector* or exoskeleton*).mp.
7	(robot* adj2 (assist* OR aid* OR mediate* or facilitate*) adj3 (therap* or interven* or rehab* or training)).mp.
8	upper extremity/
9	(upper extremit* or upper limb* or arm or shoulder or elbow or forearm or wrist or hand or finger).mp.
10	1 or 2
11	3 or 4
12	5 or 6 or 7
13	8 or 9
14	10 and 11 and 12 and 13

*, unlimited truncation; /, medical subject headings; adj2, terms within two words of each other in any order; adj3, terms within three words of each other in any order; mp, mutli-purpose.

over the eligibility of particular studies will be solved by discussion with a third reviewer (RT). The reasons for excluding study will be recorded. The selection process will be documented in a PRISMA flow diagram.[64]

Data extraction

The data of final included studies will be extracted by one reviewer (SS-U) and cross-checked by a second reviewer (BUN). If necessary, a consensus will be reached through the arbitration of a third reviewer (RT). A data extraction form will be created to record study characteristic (ie, authors, publication time and design), participant information (ie, types of CP, age and sample size), intervention delivery (ie, target of intervention, types of robotic device, modalities, duration and frequency and settings), comparator (ie, control, conventional therapy and/or other alternative treatments) and outcomes within the ICF-CY domains (ie, body function and structure and activity and participation). These items will be schemed following the PRISMA guideline.[64]

Quality of the evidence and risk of bias

The quality of the evidence in each included study will be appraised using the standard quality assessment criteria for evaluating primary research papers from a variety of fields (QualSyst tool) for quantitative studies.[69] This tool is a checklist of 14 question items on methodology and risk of bias in research. Each item is scored from 0 to 2 (ie, 'yes'=2, 'partial'=1, 'no'=0) with a maximum possible score of 28 points. Items which are not applicable to a particular study design are marked as 'n/a' and are excluded from the summary score calculation. Furthermore, studies will be ranked for the level of evidence corresponding to the Oxford Centre for Evidence-Based Medicine (OCEBM).[70]

Additionally, the Grading of Recommendations Assessment, Development and Evaluation approach will be used to evaluate the overall quality of evidence across outcomes. To obtain a procedural rating within this framework, the quality of evidence is deliberated in several aspects, starting with the study design (eg, RCT or observational studies), followed by five reasons to possibly downgrade (ie, risk of bias, inconsistency, indirectness, imprecision and publication bias), and three explanations to possibly upgrade (ie, magnitude of effect, dose of response and plausible residual confounding). A body of evidence across outcomes will be specified as high, moderate, low or very low quality.[71]

The same two independent reviewers (SS-U, BUN) will perform all critical appraisal processes. Discrepancies in judgments will be identified and resolved through discussion with a third reviewer (RT) where necessary.

Data synthesis and analysis

In the part of narrative synthesis, the results from data extraction will be reported in text and table format to summarise the characteristics and findings of the included studies. For a description of outcome measures within the ICF-CY framework, outcome data of each study will be addressed in accordance with the body function and structure and/or the activity and participation domains.

A meta-analysis will be conducted if there are sufficient data from the included studies. The risk ratio and odds ratio will be calculated for dichotomous outcome data. For continuous outcome data, the mean difference will be used to compare data measured on the same scales while the standard mean difference will be used to summarise data measured on the different scales. Heterogeneity will be evaluated by using the inconsistency index (I^2) statistic to describe the percentages of total variation across studies ($I^2 \leq 50\%$ = low heterogeneity; $I^2 > 50\%$ = moderate to high heterogeneity). Where appropriate for pooling effect sizes, a fixed effects model will be conducted when heterogeneity is low, and a random effects model will be performed when heterogeneity is moderate to high.[72 73] If unable to pool results, the data will be reported descriptively according to the classification of outcome measures. The quantitative synthesis will be analysed by using the Review Manager (RevMan) (Computer program) V.5.3, The Nordic Cochrane Centre, The Cochrane Collaboration.[74]

ETHICS AND DISSEMINATION

Since this protocol of systematic review will obtain data from relevant published academic papers without deriving from human participants, ethical approval is not required. The findings will be disseminated via a peer-reviewed journal and international conferences.

Contributors SS-U coordinated the study. SS-U and RT initiated the conception and designed the study of systematic review protocol. SS-U and BUN developed the search strategy. RT and KY provided instruction on important intellectual contributions. All authors read, provided feedback and approved the final version of the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct or reporting or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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