



Robot-assisted upper extremity rehabilitation for cervical spinal cord injuries: a systematic scoping review

Hardeep Singh, Janelle Unger, José Zariffa, Maureen Pakosh, Susan Jaglal, B. Catharine Craven & Kristin E. Musselman

To cite this article: Hardeep Singh, Janelle Unger, José Zariffa, Maureen Pakosh, Susan Jaglal, B. Catharine Craven & Kristin E. Musselman (2018) Robot-assisted upper extremity rehabilitation for cervical spinal cord injuries: a systematic scoping review, *Disability and Rehabilitation: Assistive Technology*, 13:7, 704-715, DOI: [10.1080/17483107.2018.1425747](https://doi.org/10.1080/17483107.2018.1425747)

To link to this article: <https://doi.org/10.1080/17483107.2018.1425747>



View supplementary material [↗](#)



Published online: 15 Jan 2018.



Submit your article to this journal [↗](#)



Article views: 979



View related articles [↗](#)



View Crossmark data [↗](#)





Citing articles: 9 View citing articles [↗](#)

REVIEW ARTICLE



Robot-assisted upper extremity rehabilitation for cervical spinal cord injuries: a systematic scoping review

Hardeep Singh^{a,b}, Janelle Unger^{a,b}, José Zariffa^{a,b,c} , Maureen Pakosh^a, Susan Jaglal^{a,b,d,e},
B. Catharine Craven^{a,b,f} and Kristin E. Musselman^{a,b,d} 

^aToronto Rehabilitation Institute-University Health Network, Toronto, ON, Canada; ^bRehabilitation Sciences Institute, University of Toronto, Toronto, ON, Canada; ^cInstitute of Biomaterials and Biomedical Engineering, University of Toronto, Toronto, ON, Canada; ^dDepartment of Physical Therapy, University of Toronto, Toronto, ON, Canada; ^eDepartment of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada; ^fDivision of Physical Medicine and Rehabilitation, Faculty of Medicine, University of Toronto, Toronto, ON, Canada

ABSTRACT

Purpose: To provide an overview of the feasibility and outcomes of robotic-assisted upper extremity training for individuals with cervical spinal cord injury (SCI), and to identify gaps in current research and articulate future research directions.

Materials and methods: A systematic search was conducted using Medline, Embase, PsycINFO, CCTR, CDSR, CINAHL and PubMed on June 7, 2017. Search terms included 3 themes: (1) robotics; (2) SCI; (3) upper extremity. Studies using robots for upper extremity rehabilitation among individuals with cervical SCI were included. Identified articles were independently reviewed by two researchers and compared to pre-specified criteria. Disagreements regarding article inclusion were resolved through discussion. The modified Downs and Black checklist was used to assess article quality. Participant characteristics, study and intervention details, training outcomes, robot features, study limitations and recommendations for future studies were abstracted from included articles.

Results: Twelve articles (one randomized clinical trial, six case series, five case studies) met the inclusion criteria. Five robots were exoskeletons and three were end-effectors. Sample sizes ranged from 1 to 17 subjects. Articles had variable quality, with quality scores ranging from 8 to 20. Studies had a low internal validity primarily from lack of blinding or a control group. Individuals with mild-moderate impairments showed the greatest improvements on body structure/function and performance-level measures. This review is limited by the small number of articles, low-sample sizes and the diversity of devices and their associated training protocols, and outcome measures.

Conclusions: Preliminary evidence suggests robot-assisted interventions are safe, feasible and can reduce active assistance provided by therapists.

ARTICLE HISTORY

Received 24 August 2017
Revised 26 December 2017
Accepted 5 January 2018

KEYWORDS

Spinal cord injury;
tetraplegia; robotics;
exoskeleton device; upper
extremity

► IMPLICATIONS FOR REHABILITATION

- Robot-assisted upper extremity training for individuals with cervical spinal cord injury is safe, feasible and can reduce hands-on assistance provided by therapists.
- Future research in robotics rehabilitation with individuals with spinal cord injury is needed to determine the optimal device and training protocol as well as effectiveness.

Introduction

Spinal cord injury (SCI) is a devastating, life-changing event that causes disruptions in axonal pathways and segmental spinal cord circuitry, resulting in sensory, motor and autonomic impairments [1]. Cervical SCI or tetraplegia is the most common (44–62%) of all SCIs [2,3]. Depending on the severity and location of the injury, the individual's upper extremity (UE) motor or sensory function may be impaired or completely paralyzed [4]. Restoration of UE function is a priority for individuals with tetraplegia [5]. Small improvements in UE function through rehabilitation can lead to substantial increase in function, increased independence with activities of daily living, quality of life and community integration [5,6].

SCI rehabilitation has witnessed a paradigm shift in the last few decades from the routine use of compensatory interventions to increasing implementation of recovery-based approaches [7]. This shift is likely due, in part, to our increased knowledge of neuroplasticity after SCI. As defined by Warraich and Kleim [8], neuroplasticity is “any change in neuron structure or function that is observed either directly from measures of individual neurons or inferred from measures taken across populations of neurons.” Although the mechanisms responsible for spinal plasticity are not fully understood [1], human [9] and animal studies [10] show activity-dependent spinal plasticity in response to proprioceptive feedback. There is recognition in the field that central nervous system plasticity can lead to functional improvements, as well as

unwanted effects such as allodynia, neurogenic pain, autonomic dysreflexia and spasticity [11]. Current rehabilitation approaches, such as movement training with robotic devices, aim to promote adaptive plasticity and functional improvements. To date, the majority of SCI robotic research has focused on lower extremity training, with less attention to UE training using robotics [5].

Rehabilitation robotics is a discipline that develops robots for specific therapeutic or assistive functions. The primary purpose of therapeutic robots is to provide therapy for physical and/or cognitive impairments and facilitate recovery by augmenting “the clinician’s toolbox” [12,13]. This is distinct from assistive robots which are used to compensate for lost function [12]. Many in the field believe that therapeutic robotic devices can facilitate plasticity after SCI [14,15]. The robotic device’s ability to deliver high volume, repetitive movements and quantify training outcomes [15–18] make them attractive tools for rehabilitation. These devices should include the following features: safety, ability to quantify performance, cost-efficient, comfort, varying modes to allow for training customization and to allow natural and free movement while using the device [19–22]. Altogether, these features may ultimately lead to reduction in healthcare personnel costs [7]. Nevertheless, constructing devices that can successfully meet the many aforementioned specifications of an ideal rehabilitation tool is complex.

While therapeutic robotics have been around since the 1990s, no standardized protocols have yet been established for use in SCI rehabilitation. Several systematic reviews have investigated the effectiveness of robot-assisted UE stroke therapy and concluded that it provides improvements that are similar to, or greater than conventional rehabilitation [23–26]. A Cochrane review by Mehrholz et al. [25] found robotic training resulted in improvements in performance of activities of daily living among individuals with stroke; whereas a review by Veerbeek et al. [26] concluded no significant improvements in performance of activities of daily living.

Celik et al. [27] published a review in Turkish on robot-mediated SCI rehabilitation in 2015; however, the review does not have an English translation precluding generalizability of the findings. Furthermore, the authors’ search strategy (e.g. criteria, databases) and inclusion/exclusion criteria were not made explicit in the review.

The current review seeks to provide a comprehensive overview of the range and nature of current robotic interventions and to further investigate the potential applications of therapeutic robotic interventions in UE spinal cord rehabilitation using a systematic scoping review. Specifically, this review seeks to address the following objectives:

- Determine how effective and feasible are robotic-assisted interventions in UE rehabilitation programs for individuals with tetraplegia.
- Describe characteristics (i.e. age, gender, level of injury, motor score, time since injury) of participants with tetraplegia for whom robotic therapy has been studied.
- Describe what robotic training protocols have been employed to restore motor function in individuals with tetraplegia.
- Based on the currently available data, highlight considerations that future studies should take into account with respect to robotics being utilized for the UE in cervical SCI rehabilitation.

Materials and methods

Data sources and searches

Given the heterogeneous nature of the research questions, a systematic scoping review methodology [28,29] was used. Systematic

scoping reviews have previously been applied when interventions are heterogeneous and when the results will be descriptively analyzed [28,29]. This review was conducted following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) checklist. PRISMA is a 27-item checklist that provides guidance for reporting evidence in systematic reviews [30]. Prior to and including 7 June 2017, a search was conducted with assistance from an expert medical librarian (MP) on the following electronic databases: Medline, Embase, PsycINFO, Cochrane Central Register of Controlled Trials (CCTR), Cochrane Database of Systematic Reviews (CDSR), Cumulative Index of Nursing and Allied Health Literature (CINAHL) and PubMed. The search strategies (Appendix 1) were following the participants, interventions, comparators and outcomes [30] method and utilized a combination of valid subject headings, as appropriate for each database, and key free text terms in order to extract all relevant records. No date or language limitations were imposed and the reference lists of included studies were manually searched. The objectives, inclusion criteria and methods for this review were specified in advance and documented in a registered protocol Prospero on 20 December 2016 (registration # CRD42016053221) [31].

Study selection

Inclusion

For this review, a therapeutic robot was defined as a device that facilitates recovery and is used to “augment the clinician’s toolbox in order to deliver meaningful restorative therapy” [12].

Given the limited available literature on this topic, and to ensure consideration of all relevant studies, the research design and outcome criteria were kept broad. Since randomized control trials (RCTs) employing developing technologies as interventions are limited [32], the inclusion of multiple types of studies including case studies and case-series was warranted [33]. For these reasons, we have included all full-text RCTs, non-randomized controlled trials (non-RCTs), cohort studies, pre-post and post-interventions, case series, case control studies and case reports in this review. Studies meeting the following criteria were included: interventions with a therapeutic robotic device to assist UE training in individuals with tetraplegia due to cervical SCI of traumatic or non-traumatic etiology. Studies using concurrent interventions were included if at least one intervention employed a therapeutic robot. All reported outcomes were considered.

Exclusion

Non-intervention articles, conference abstracts, book chapters, gray literature, protocol papers, animal studies, and/or articles that did not include participants with tetraplegia were excluded. Interventions employing the assistive use of robots and therapeutic robots for lower extremity rehabilitation were excluded. As we intended to examine the therapeutic use of robotic devices, home-based or self-directed intervention programs (i.e. without a therapist present during training) were excluded. Home-based/self-directed interventions also raise concerns about appropriate administration and adherence to robotic training protocols.

Two authors (HS and JU), independently screened the title and abstracts for each article based on the predefined inclusion and exclusion criteria using Covidence[®] online systematic review software [34]. Next, full text screening was conducted to determine inclusion. Articles not meeting the predefined inclusion criteria were excluded. Disagreements during the screening process were resolved through discussion.

Quality assessment

Two authors (HS and JU) independently conducted quality assessments for the articles selected for inclusions using the Eng et al. [35] modified Downs and Black checklist for RCTs and non-RCTs. Any disagreements in scoring were resolved through discussion. The Down's and Black checklist meets accepted reliability standards; with strong internal consistency scores, high test and retest reliability for all subscales, good inter-rater reliability and possesses strong methodological ratings [36,37]. The checklist has been previously applied to several other rehabilitation intervention reviews [35,38,39]. The checklist has 27 questions covering five domains: (1) reliability, (2) external validity, (3) internal validity, (4) confounding and selection bias and (5) the power of the study. An overall score out of 28 is generated as well as sub-scores in each of the categories, where a higher score corresponds to higher methodological quality [36]. Overall scores <11 points indicates "poor" quality, 11–19 points indicates "moderate" quality and >19 points indicates "good" quality [40].

Data extraction and synthesis

The following information was abstracted from included articles: author details (name and country); participant characteristics (age, gender, level of injury and American Spinal Injury Association Impairment Scale (AIS) classification according to the International Standards for the Neurological Classification of SCI (ISNCSCI), time since injury); study characteristics (design, setting, blinding, control groups); training characteristics (number, length and frequency of training sessions, robotic device and features, co-interventions); outcomes and adverse effects; study limitations; and considerations for future research identified by authors.

As studies used various rehabilitative training methods and the outcomes measured were gathered from heterogeneous populations (i.e. differences between level of function and time since injury), results could not be statistically pooled and effectiveness could not be determined. Rather, comprehensive details of the studies' characteristics and their interventions are provided in the results section below. Outcome measures are categorized based on the International Classification of Functioning, Disability and Health, which is a framework for organizing information on health and functioning [41]. For the purpose of this review, outcome measures categorized in the body functions and structures category examine functioning at the level of the body [41]. Outcome measures at the activity level examine "execution of a task or action by an individual" while participation level measures refer to, "involvement in a life situation" [41]. Also, it is important to note that some outcome measures fit into more than one category.

Results

Study identification

A total of 302 articles were identified from the following databases: PsycINFO ($n=8$), Medline ($n=101$), Embase ($n=144$), CINAHL ($n=27$), CDSR ($n=2$), CCTR ($n=5$) and PubMed ($n=15$) and 118 duplicates were removed. Two articles were located through hand searching. Title and abstracts were screened for 186 articles, excluding 155 articles. A full text review was conducted for 31 articles. Nineteen articles were excluded after the full text review for the following reasons: ineligible population ($n=3$), ineligible intervention (i.e. robot for compensation or no robotic device) ($n=11$), not an intervention ($n=4$), and ineligible setting

($n=1$) (Figure 1). In total, 12 articles met the study inclusion criteria (Table 1).

Methodological quality

Table 2 and supplementary online material outline the results of the evaluation of methodological quality using the modified Downs and Black checklist ($n=12$). The included RCT [42] scored "good" for methodological quality (i.e. 20/28). This RCT failed to receive scores for being representative of the entire population, facility, describing/accounting for losses to follow-up and study power. For non-RCTs ($n=11$), the average total score was 11.6 ± 2.5 (range 8–17) [19,20,22,43–50]. In terms of study quality, scores ranged from four to eight [19,20,22,43–50] from a total possible score of 10. Six of 11 non-RCTs [22,43–45,47,49] received points for external validity. Overall, a high selection bias was noted in the non-RCTs with the most common issue being lack of blinding and randomization. Studies also had insufficient power to detect significant effects. Overall, three non-RCTs [19,46,50] scored "poor" for methodological quality, while eight scored within the "moderate" range [20,22,43–45,47–49].

Study design characteristics

Tables 1 and 2 list the details abstracted for each study. Table 2 was adopted from Chen and Howard [51] and modified to the review intent. The following study designs are included in this review: one randomized clinical trial, six case series, five case studies. Additionally, sample sizes in these studies varied in range: $n=17$ [49], $n=15$ [43], $n=10$ [47,50], $n=9$ [42], $n=5$ [22], $n=2$ [19], $n=1$ [20,44–46,48]. The RCT compared control groups receiving only robotic therapy to the intervention group receiving transcranial direct current stimulation (tDCS) and robotic therapy [42]. To test the efficacy of a new "assist-as-needed" robot control feature, Frullo et al. [49] divided participants into two groups – assist-as-needed group, which received automatically adjusted assistance and resistance, and a subject triggered group, which received training where assistance and resistance were not automatically adjusted. Another study used participants' untrained arm to measure training effectiveness between conventional therapy (untrained arm) to robotic therapy (trained arm) [43]; in the remaining studies, no control groups were used. Studies were conducted in the USA [19,20,42,44–47,49,50], Canada [43], Japan [48] and the Netherlands [22].

Participants

A total of 73 participants were recruited and 62 participants completed training across the 12 studies of whom 46 men and eight women completed the training. One study that recruited 10 participants (eight men, two women) [50], did not specify the sex of their drop outs. Sixteen participants had motor complete injuries (AIS A and B) [22,43,47] and 46 had motor incomplete injuries (AIS C and D) [19,20,42–47,49,50]. The participants' ages ranged from 17–75 years [19,20,22,42–50] and participants were in the subacute [43,44,48] or chronic [19,20,22,42,45–47,49,50] stages of recovery. Time since injury ranged from 21 days to 16 years [19,20,22,42–50] across studies.

Exclusion criteria reported in the studies were: individuals experiencing severe UE pain [42,43], exercise intolerance, severely limited range of joint motion [42], irreversible muscle contractures [22,42] and/or an inability to tolerate upright sitting for a minimum of 30 min [43]. Further, individuals with cognitive

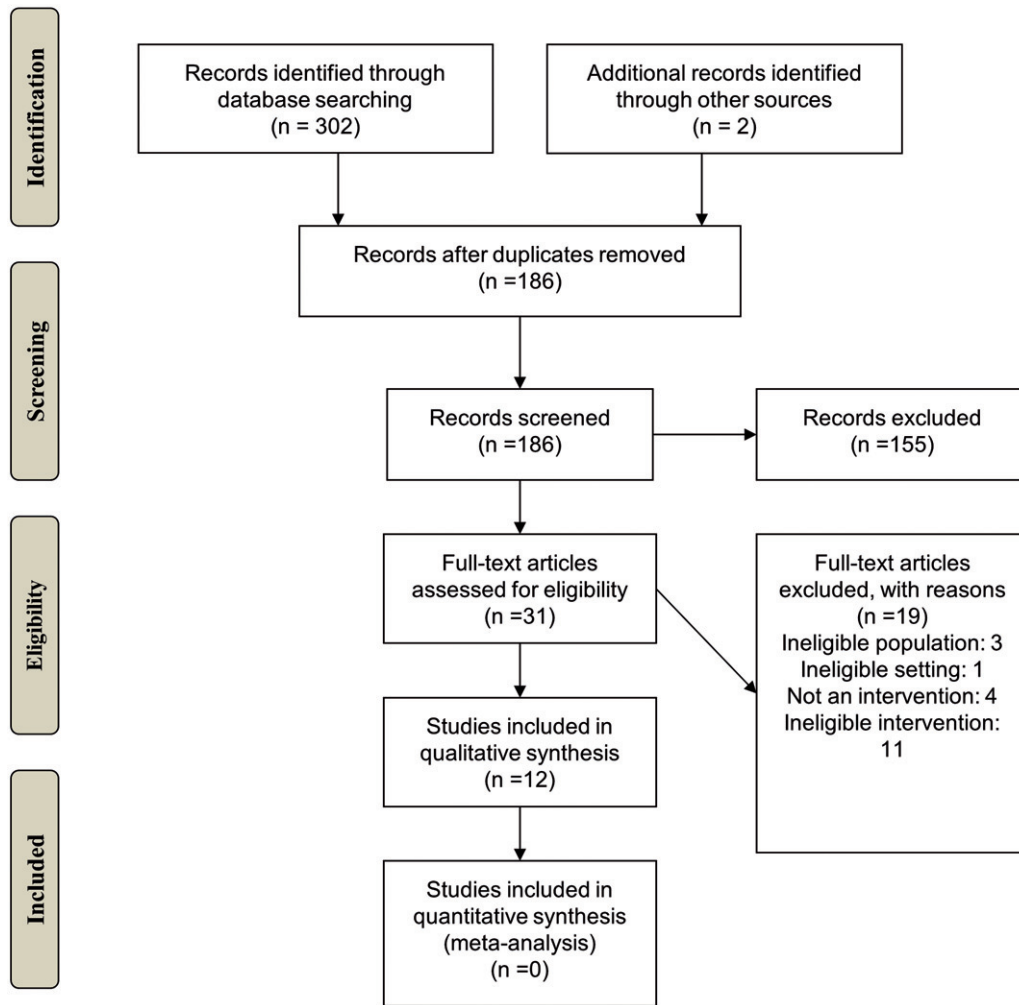


Figure 1. PRISMA flow diagram.

Table 1. Study design details.

Study	Country	Setting	Design
Kadivar et al. [19]	USA	Outpatient	Case series
Pehlivan et al. [20]	USA	Outpatient	Case study
Vanmulken et al. [22]	Netherlands	Outpatient	Case series
Yozbatiran et al. [42]	USA	Outpatient	Clinical RCT
Zariffa et al. [43]	Canada	Inpatient	Case series
Sledziewski et al. [44]	USA	Inpatient	Case study
Yozbatiran et al. [45]	USA	Outpatient	Case study
Yozbatiran et al. [46]	USA	Outpatient	Case study
Cortes et al. [47]	USA	Outpatient	Case series
Hoei et al. [48]	Japan	Outpatient	Case study
Frullo et al. [49]	USA	Outpatient	Case series
Fitle et al. [50]	USA	Outpatient	Case series

impairments, concurrent neurological or neuromuscular conditions [42,43], individuals currently using central nervous system medications [42], those with prior participation in robotic training for the UE [49] were excluded from the robotic interventions. Five of the 12 studies found participants prematurely dropped out, with dropout rates ranging from 11–40% [22,42,43,49,50]. The following reasons were cited for dropout: transportation issues [42], health issues unrelated to training [22], busy schedule, the combination of a busy schedule and secondary health complications, logistical reasons [49] and a lack of interest in training [43]. Those with severe impairments, and who were at the longest time post-injury, were the least motivated during training, as evidenced by the

Intrinsic Motivational Inventory [22]. Fitle et al. [50] did not specify the reasons for dropout from their intervention.

Intervention

The robotic devices and training protocols employed were variable across the 12 studies. Interventions included one of the following robots in their training protocols: RiceWrist (Rice University, USA) ($n=2$) [19,45], RiceWrist-S (Rice University, USA) ($n=1$) [20], MAHI Exo-II (Rice University, USA) ($n=3$) [46,49,50], MAHI Exo-II + tDCS (Rice University, USA) ($n=1$) [42], Haptic Master (HM) ($n=1$) [22], TMS + InMotion 3.0 Wrist Robot (Interactive Motion Technologies Inc., USA) ($n=1$) [47], Armeo®Spring (Hocoma AG, Switzerland) ($n=1$) [43], ReoGo (Motorika Medical, Caesarea, Israel) ($n=1$) [44], and Reaching Robot ($n=1$) [48]. Descriptions of the robots and training modes used in the protocols of selected studies are provided in Table 3. Five robots are exoskeletons [19,20,42,43,45,46,49,50], which align with and allow individual actuation or support of targeted joints [20], while three robots are end-effectors [22,44,48], which contact users at the distal part of their limb [22]. Most robots featured adjustable modes allowing them to be tailored to a user's abilities.

Two studies with subacute participants in inpatient settings received concurrent therapy [43,44]. Four studies in outpatient settings reported no concurrent therapy during their intervention

Table 2. Interventions, participant characteristics, and Down's and Black methodological quality scores.

Study	Sample size	Participant characteristics	Intervention dose	Co- therapy	Down's and Blacks score
Kadivar et al. [19]	2 (M,F)	Chronic C2, C4 AIS C and D Age: 24, 27 yrs TSI: 6.5 months	RiceWrist 1–3 hr × 3 days/week × 7 and 10 sessions	NR	9 (P)
Pehlivan et al. [20]	1 (M)	Chronic C3–C5 AIS C Age: 45 yrs TSI: 83 months	RiceWrist 1 hr × 4 days/wk × 3 wks	No	11 (M)
Vanmulken et al. [22]	5 2 drop outs (3M)	Chronic C5–C7 AIS A(1), B(2) Age: 25–45 yrs TSI: 3.5–15.5 yrs	Haptic Master 1 hr × 3 days/wk × 6 wks	NR	12 (M)
Yozbatiran et al. [42]	9 1 drop out (7M,1F)	Chronic C3–C7 AIS C(3), D(5) Age: 36–62 yrs TSI: 7–244 months	MAHI Exo-II 10 sessions over 2 wks	No	20 (G)
Zariffa et al. [43]	15 3 drop outs (11M,1F)	Subacute C4–C6 AIS A(2), B(4), C(1), D(5) Age: 19–75 yrs TSI: 21–173 days	Armeo Spring 1 hr × 3–5 days/wk × 6 wks	CT	17 (M)
Sledziewski et al. [44]	1 (M)	Subacute C4 AIS D Age: 51 yrs TSI: 26 days	ReoGo 2 hr × 5 days/wk × 4 wks	OT	11 (M)
Yozbatiran et al. [45]	1 (M)	Chronic C4 AIS D Age: 24 yrs TSI: 6.5 months	RiceWrist 3 hr × 10 consecutive days	No	11 (M)
Yozbatiran et al. [46]	1 (F)	Chronic C2 AIS C Age: 28 yrs TSI: 29 months	MAHI Exo-II 3 hr × 3 days/wk × 4 wks	No	10 (P)
Cortes et al. [47]	10 (8M,2F)	Chronic C4–C6 AIS A(3), B(4), C(1), D(2) Age: 17–70 yrs TSI: 2–8 yrs	InMotion 3.0 Wrist robot 1 hr × 3 days/wk × 6 wks	NR	14 (M)
Hoei et al. [48]	1 (M)	Subacute C3–C6 AIS NR Age: 66 yrs TSI: 3 months	Reaching Robot 40 min × 7 days/wk × 2 wks	NR	11 (M)
Frullo et al. [49]	17 3 drop outs (12M, 2F)	Chronic C3–C8 AIS C–D Age: mean 53.5 yrs TSI: mean 16 yrs	MAHI Exo-II 1.5 hr × 10 sessions	NR	14 (M)
Fitle et al. [50]	10 2 drop outs (8M, 2F)*	Chronic C2–C6 AIS C–D Age: NR TSI: NR	MAHI Exo-II 2h × 12 sessions	NR	8 (P)

M: male; F: female; TSI: time since injury; AIS: American spinal injury association impairment scale; MAHI: Mechatronics and Haptic Interfaces Lab; yrs: years; wks: weeks; NR: not reported; CT: conventional therapy; OT: occupational therapy; (P): poor; (M): moderate; (G): good; *Fitle et al. did not report sex of participants that dropped out.

[20,42,45,46] and six studies did not specify whether participants received concurrent therapy [19,22,47–50]. Overall, training protocols varied in intervention length, with the longest being six weeks [22,43,47], followed by four [42,44,46,49], three [20] and two weeks [19,45,48,50]. The length of training sessions ranged from forty minutes [48] to three hours [19,42,45,46]. Unilateral training was conducted in seven studies [20,42–44,47–49]. While some interventions were conducted in the active-constraint modes [42,50], others adjusted robot training modes to suit the participant during the training sessions [19,20,22,44,45,49]. All training interventions were designed to provide a high-frequency of repetition of movements using various robotic-assisted training strategies.

Supervision

Robotic training sessions were administered and supervised by occupational therapists [22,42,44,48,49] or physical therapists [19,20,50].

Passive support

The Armeo®Spring provided anti-gravity weight support (no actuators) of the participant's shoulder, elbow and forearm during training. Training difficulty was adjusted by altering the range of motion required to control virtual reality tasks, adjusting the amount of anti-gravity weight support provided by the robot and increasing/decreasing the number of repetitions [43]. Similarly, the Reaching Robot is an "arm weight bearing device" that assists with repetitive UE reaching using a suspension wire to facilitate reaching movements [48]. The Reaching Robot was combined with continuous low-amplitude neuromuscular electrical stimulation to the proximal upper extremity [48].

Robot assistance

Assistive modes were selected for training with participants experiencing high levels of UE pain [44] or weakness [46]. In the assist mode, the robot provided assistance with either the entire movement or with initiating or completing movements. The level of

Table 3. Description of robots.

Robot name/type	Features	Degrees of freedom	Mode
<i>RICEWRIST</i> [19,45]	Exoskeleton	4	Passive Triggered
<i>REOGO</i> [44]	End-effector	3	Active-constraint Guided Initiated
<i>HAPTIC MASTER</i> [22]	End-effector	3	Passive Active-assisted Active
<i>RICEWRIST-S</i> [20]	Exoskeleton	3	Not specified
<i>MAHI EXO-II</i> [42,46,49,50]	Exoskeleton	5	Passive Triggered Active-constraint
<i>ARMEOSPRING</i> [43]	Exoskeleton	5	No actuators; adjustable anti-gravity weight support of arm
<i>INMOTION 3.0 WRIST ROBOT</i> [47]	Exoskeleton	3	Unassisted Forceful Resisted
<i>REACHING ROBOT</i> [48]	End-effector	NR	No actuators; adjustable motor-load relieving device [47]

*NR: not reported; MAHI: Mechatronics and Haptic Interfaces.

assistance varied based on the participant's capabilities, levels of fatigue and tolerance. For example, the computer software in the ReoGo protocol allowed participants to progress from the guided (full assistance) to initiated levels with the user initiating and the robot completing the rest of the movement [44]. Comparably, the MAHI Exo-II robot operated in triggered mode, in which the participant was required to overcome a specific threshold after which the robot assisted in completing the motion. Frullo et al. [49] created a novel robotic controller which automatically and continually adjusts the level of assistance provided by the MAHI Exo-II.

Robot resistance

Robot resistance was selected for participants who possessed adequate strength to actively perform the movement. Fitle et al. [50] operated the robot only in the active-constrained mode. In this mode, the robot exerts a force field, which is proportional to movement velocity of the particular joint [50]. Movement velocity, fatigue and pain were important considerations to adjusting the level of resistance applied [20,49,50].

Combination (assistance and resistance)

Some studies used multiple training modes in their protocols [19,22,45–47,49]. In circumstances where the participant was unable to complete the full motion, the robot provided increased assistance while removing resistance. Using a combination of assistance and resistance, Cortes et al. [47] aimed for 1000 wrist movements per session. Similarly, another protocol trained for three hours per day using multiple modes to induce single joint exercises [45]. Vanmulken et al. [22] employed task-oriented training using the Haptic Master in which tasks were broken down into subcomponents consisting of repetitive training. The Haptic Master provided assistance if the individual was unable to initiate or complete the activity [22].

Motivation

Visual performance feedback, virtual reality games, target hitting and haptic feedback were provided with the aim of motivating participants during their training [19,20,22,43–47,49,50]. In one study, participants selected functional, real-life activities for training, which was believed to increase motivation during training [22].

Limitations of robots

Two studies reported limitations of the devices used in their training protocols. Vanmulken et al. [22] found that the HM had a restricted space in which movements could be performed, thus preventing fluid movement. A limitation of the ReoGo was that it restricted users' full range of motion (ROM), specifically, reducing shoulder flexion to 80 degrees and shoulder abduction to 90 degrees [44].

Outcome measures

A variety of outcome measures were used to measure the effectiveness of interventions. Findings from studies are summarized in Table 4.

Most outcome measures are categorized as a body structure/function and activity level measures. The most commonly used measures included: the Jebsen Taylor Hand Function Test (JTHFT) [19,20,42,45,46,50], Action Research Arm Test (ARAT) [19,42,45,48,49], ASIA upper extremity motor scores (UEMS) [20,42,44–47], ROM [43,44,48], grip strength, pinch forces [20,43,45,49], and the Modified Ashworth Scale (MAS) [42,47–50]. The Amount of Use Scale of the Motor Activity Log (AOU-MAL) [42] measured both activity and participation levels.

Effectiveness

Three studies found statistically significant improvements in robotic measurements of smoothness of movements [19,20,47]. Other improvements in body function resulting from training included: increased ROM [44,48], pinch and grip strength [20,45,49], UEMS [42,44–46] and muscle strength [22]. Individuals with baseline partial hand function or mild-moderate impairments showed the greatest improvements on outcome measures [19,43,45,46]. Performance (i.e. activity level) improvements were reported in nine studies [19,20,22,42,44–46,48,50] and one specified training effects were observed after 12 treatment sessions [46]. Improvements in participants' functional independence after training were also noted in two studies [44,45].

To the contrary, studies reported little to no clinically significant improvements in muscle strength [20,42,45,47], sensory function [44], corticospinal excitability [47], grip strength [45] and ROM [43]. Frullo et al. [49] also found only weak gains in clinical

Table 4. Results on outcome measures after training.

Body structure and function																			Activity level							Participation	
Cortical excitability	Fs	UEMS	Sensory	ROM	Grip	Pinch	MAS	ICSHT	VLT	GRASSP	FIM	JTHFT	SCIM	ARAT	SIAS	STEF	CUE	USE									
Kadivar et al. [19]	+ (m) nc (s)											+															
Pehlivan et al. [20]	+	nc			+	+						+		nc													
Vanmulken et al. [22]																											
Yozbatiran et al. [42]		+			nc		nc	nc	+	+		+	nc														
Zariffa et al. [43]																											
Sledziewski et al. [44]		+	nc	+	+	+					+	+					+										
Yozbatiran et al. [45]		+ (s) nc (m) + (m) nc (s)			nc (s)																						
Yozbatiran et al. [46]												+	nc (s)														
Cortes et al. [47]	nc	+	nc																								
Hoei et al. [48]				+	+	+		nc								+	+										
Frullo et al. [49]								nc		+				nc													
Fitte et al. [50]								nc				+		+													

*Improvements did not last at two-month follow-up
(m): mild-moderately impaired side; (s): severely impaired side; nc: no change; +: change; Fs: smoothness of movement; UEMS: upper extremity motor score; ROM: range of motion; MAS: Modified Ashworth Scale; ICSHT: International classification for surgery of the hand in tetraplegia; VLT: Van Lieshout test for UE function in tetraplegia; GRASSP: graded and redefined assessment of strength, sensibility and prehension; FIM: functional independence measure; JTHFT: Jebsen Taylor hand function test; SCIM: spinal cord independence measure; ARAT: action research arm test; SIAS: knee-mouth test and the finger test of the stroke impairment assessment set; STEF: simple test for evaluating hand function; CUE: capabilities of upper extremity instrument; USE: usefulness, satisfaction and ease-of-use questionnaire; AOU-MAL: action research arm test

outcomes and found no demonstrated gains in arm function after the intervention. Three authors explained that these insignificant improvements were possibly due to the short duration/dose of training [43,47,49].

Studies concluded that their results provided insight into the feasibility and effectiveness of robotic-assisted training for SCI rehabilitation [19,20,45,46,48,50]. Yozbatiran et al. [42] concluded that combination therapy showed potential to improve UE function, in comparison to only robotic training. Sledziewski et al. [44] found supplementing conventional therapy with robotic training should warrant further investigation. Zariffa et al. [43] concluded while robotic-assisted training is feasible in an inpatient setting, it offers few functional benefits when compared to conventional training. Albeit, robot-assisted therapy was successful in reducing the amount of active therapist time during training sessions by 25%+/-11% and had no adverse training effects [43]. Two studies specified the set-up time required for participants to be arranged with the device, which ranged from 5 [49] to 10 [20] minutes per participant. In terms of feasibility, no significant adverse effects interfering with training such as pain, discomfort or fatigue were reported [19,20,22,42,44–50].

Discussion

Given the inconsistent quality of studies, variable study designs and low-sample sizes, the results of this systematic scoping review must be interpreted with caution. Based on the results and conclusions drawn from these studies, the use of robots for UE SCI rehabilitation appears to be feasible in terms of safety and tolerance and has some beneficial utility in both inpatient and outpatient SCI rehabilitation. However, the effectiveness of robotic training was inconclusive, which highlights the need for more rigorous research with larger sample sizes to inform the development of effective training protocols. This review allowed us to critically assess, describe and synthesize current literature to inform future study design.

Although RCTs serve as the “gold standard” for all scientific inquiry, including healthcare interventions [52], their practicality in rehabilitation interventions has been questioned [53]. RCTs can be costly, time-consuming and require a large evidence base before investors are willing to fund them [54]. Therefore, preliminary studies such as the ones included in this review can provide justifications for more rigorous research to be conducted using larger sample sizes [55].

The following are our recommendations for future studies. When designing or selecting appropriate robotic devices for rehabilitation, clinical utility and costs of robotic devices are two important factors to consider [43]. Protocols should be reproducible and systematic in building up repetitions and resistance [44] and include higher frequency and dose of robotic training [22,43,47,49]. We strongly support incorporating new evidence and collaboration with perspectives from multiple stakeholders (i.e. users, front-line clinicians, scientists, engineers) in the design of robotic devices and protocols. In terms of study design and participants, more rigorous study designs, with larger sample sizes and homogenous groups should be employed. Reporting reasons for dropping out of training interventions can guide the development of more effective future protocols. Furthermore, to determine which groups would reap the greatest benefits from training, reporting screening to enrolment ratios and discriminating the effectiveness of training protocols between heterogeneous groups of baseline function are important [20,43]. Finally, the use of measures that are more sensitive to small motor or functional

changes when training individuals with severe limitations [20,43] is recommended.

Knowledge gap – clinical utility of robotic devices

Clinical utility refers to the relevance and usefulness of an intervention [56] and is important for the translation from research to clinical practice. Uncertainty regarding optimal robot design [57] is currently limiting the clinical utility of robotic interventions in SCI rehabilitation. Many variables must be considered, such as the device's ability to allow full and fluid movement [22], cost [58], comfort [19] transportability, and its ability to provide accurate quantitative measurements [20,58]. Dijkers et al. [59] reported that if set-up time takes longer than five minutes, therapists may abandon the device. Therefore, another factor to consider is set-up time, which includes the positioning requirements. Devices that require users to transfer out of their wheelchair would increase set-up times, which may be a potential barrier to the uptake of robotic devices.

Related to clinical utility is economic cost. In regards to the potential advantages of robot-assisted therapies for reducing healthcare costs, Zariffa et al. [43] concluded robot-assisted therapy was effective in reducing active, hands-on, therapist time. As robots become more prevalent in clinical practice, the therapist may take on more of a supervisory role [12,60]. Studies should include economic analyses to determine the economic benefits of utilizing robots in clinical practice.

Technology designers may consider user-centered designs, which place the end users as central to the design of technologies [61] when developing new or modifying existing robots. In line with user-centered design principles, future direction should involve neuroscientists, engineers, clinicians and individuals with SCI working together rather than independently to identify key requirements needed for robots and to evaluate existing robots to guide improvements. Our recommendation is to create and study robots that possess high clinical utility, while reducing costs, enabling faster set-up time and creating devices that enable multi-joint training [18].

Knowledge gap – optimal training protocols

As previously described, a variety of devices were used in the interventions included in this review. Devices had different features and supported different UE movements. Furthermore, since the training protocols were adjusted based on the performance of each user, most protocols are difficult to reproduce.

At this juncture, the best training robot, optimal dose and frequency of robotic training remains undetermined [46]. In order to facilitate neuroplasticity, training should be within the optimal intensity level, specific to each user, and should maximize voluntary movements [1]. Adjusting the modes of the robot, can allow the robotic training to be tailored to varying levels of function. In comparison to exoskeleton robots, end-effectors offer less control for manipulating specific joints. For this reason, exoskeletons have been preferred for SCI rehabilitation as they can allow manipulation of individual joints and precisely measure isolated joint movements [20]. Moreover, to identify optimal training intensity, it is important to develop and fine-tune measures to monitor fatigue as levels of fatigue can interfere with performance [14,62]. Considering these factors, we recommend rehabilitation robot protocols to be informed by the most up-to-date evidence on motor learning and plasticity after neurological injuries, and to advocate for multidisciplinary teams that can use robotic devices to put those theories to the test in a rehabilitation context.

Knowledge gap – optimal participants

Uncertainty exists concerning when to introduce robotic training (subacute or chronic stage); however, there is evidence from robotic training of lower extremities suggesting early training may be advantageous [63–65]. The studies analyzed in this review found robotic training was feasible for both subacute [43,44,48] and chronic groups [19,20,22,42,45–47,49,50]. Most protocols were conducted with chronic participants, which eliminate improvements attributable to spontaneous recovery, which can occur up to 18 months post-SCI [66,67]. Based on the “gold standard” drop-out rate of less than 20% for interventions [68], dropout rates were high in one intervention with chronic participants with SCI where two of the five (40%) participants dropped out [22]. Our first recommendation is for studies to report the reasons cited by participants for dropping out of training. This information will serve researchers and clinicians designing future protocols.

Studies included in this review indicated training was more effective in individuals who possessed low spasticity [47] and those that retained some residual motor function [19,43]. This is consistent with previous studies which found flaccid paralysis [69,70] and/or increased tone [10] interfered with training. A majority of the participants were AIS C and D, which generally have the greatest potential for recovering UE function [71]. Since level of function can vary considerably in tetraplegia [43,72,73], our second recommendation for future research is to include homogeneous participants (i.e. similar AIS level, baseline hand motor function, time since injury and motivational level) [42,43,47]. Larger sample sizes is our third recommendation, as large samples are needed to demonstrate statistical significance in order to illustrate the technology's effectiveness in clinical applications [20,22,42,47].

Studies in this review excluded those with increased spasticity, shoulder pain, exercise intolerance and an inability to sit upright for the training duration. Since a significant proportion of individuals with tetraplegia experience spasticity (78%) [74] as well as shoulder pain (46%) [75], we therefore recommend that studies report the screening to enrolment ratios to demonstrate the number of individuals with tetraplegia for whom the intervention was appropriate.

Knowledge gap – appropriateness of outcome measures

No agreement has been established regarding what constitutes appropriate outcome measures to assess UE function in individuals with tetraplegia. Measures that are sufficiently sensitive to capture small changes, and can pinpoint changes in specific muscle groups are desired [76].

Small improvements of UE function after tetraplegia could significantly increase daily functioning and enhance overall quality of life [5,6]. In selecting appropriate outcome measures, several factors must be considered, such as a tool's sensitivity to detect change [77]. Results that provide accurate measurements are particularly important when working with individuals with severe motor limitations, where small improvements can be potentially missed by less sensitive outcome measures [78,79]. Robotic devices can provide objective performance measures, however, given the diversity in movement supported by robots, their measurements become difficult to compare. At this time, only a few robotic measures have been validated (i.e. RiceWrist-S) [20]. Future research should continue to validate robotic assessments to allow for more precise measurements of effectiveness from interventions [43]. The use of a combination of outcome measures are recommended (i.e., body structure and function (Graded Redefined

Assessment of Strength, Sensibility and Prehension) activity level (Spinal Cord Independence Measure) and participation level (Impact on Participation and Autonomy Questionnaire) [76] agreement on what constitutes the best available outcome measures is recommended as it could improve evidence building for UE interventions in SCI [76].

Limitations

Reviews are inherently biased if the included studies provide data of a lower quality [80]. As such, this review is limited by the quality of relevant research studies investigating this particular method of rehabilitation training. Assessing methodological quality and risk of bias in non-RCTs is challenging [81]. Given that most studies included in this review were case series/studies, had small or inadequate sample sizes, and few studies had control groups, conclusions cannot be drawn about effectiveness and generalizability of the review results. Pilot studies are susceptible to bias and rank low on the hierarchy of evidence, but can still guide improvements for future research [82,83]. Lastly, the variability in study designs, outcome measurement tools and training protocols used in these studies prevented statistical pooling of results.

Conclusions

This systematic scoping review provided a detailed description of studies that have employed robotics in a therapeutic capacity to assist in UE rehabilitation for individuals with tetraplegia. Currently, the integration of technological advances into SCI rehabilitation is still largely experimental, yet its potential benefits in clinical applications are not to be ignored. Even so, future research is required to better determine which robotic devices are best suited, what the optimal training protocols for robot-assisted rehabilitation programs should be, as well as their overall effectiveness.

Disclosure statement


The authors report no conflicts of interest.

Funding

This work was supported by the Craig H. Neilsen Foundation under Grant [440070]; and Ontario Neurotrauma Foundation under Grant [2013-SCI-RECOV2-974] to KEM. SJ is supported by the Toronto Rehabilitation Institute-University Health Network Chair at the University of Toronto.

ORCID

José Zariffa  <http://orcid.org/0000-0002-8842-745X>

Kristin E. Musselman  <http://orcid.org/0000-0001-8336-8211>

References

- [1] Lynskey JV. Activity-dependent plasticity in spinal cord injury. *J Rehabil Res Dev*. 2008;45:229–240.
- [2] Fehlings M, Singh A, Tetreault L, et al. Global prevalence and incidence of traumatic spinal cord injury. *Clin Epidemiol*. 2014;6:309–331.
- [3] Milby AH, Halpern CH, Guo W, et al. Prevalence of cervical spinal injury in trauma. *Neurosurg Focus*. 2008;25:E10
- [4] Dietz V, Fouad K. Restoration of sensorimotor functions after spinal cord injury. *Brain*. 2014;137:654–667.

- [5] Anderson KD. Targeting recovery: priorities of the spinal cord-injured population. *J Neurotraum*. 2004;21:1371–1383.
- [6] Snoek GJ, IJzerman MJ, Hermens HJ, et al. Survey of the needs of patients with spinal cord injury: impact and priority for improvement in hand function in tetraplegics. *Spinal Cord*. 2004;42:526–532.
- [7] Riener R. Rehabilitation robotics. *FNT in Robotics*. 2013;3:1–137.
- [8] Warraich Z, Kleim JA. Neural plasticity: the biological substrate for neurorehabilitation. *PMR*. 2010;2:S208–S219.
- [9] Dietz V. Human neuronal control of automatic functional movements: interaction between central programs and afferent input. *Physiol Rev*. 1992;72:33–69.
- [10] Pettersson LG, Lundberg A, Alstermark B, et al. Effect of spinal cord lesions on forelimb target-reaching and on visually guided switching of target-reaching in the cat. *Neurosci Res*. 1997;29:241–256.
- [11] Brown A, Weaver LC. The dark side of neuroplasticity. *Exp Neurol*. 2012;235:133–141.
- [12] Krebs HI, Volpe BT. Rehabilitation robotics. *Handb Clin Neurol*. 2013;110:283–294.
- [13] Lum PS, Godfrey SB, Brokaw EB, et al. Robotic approaches for rehabilitation of hand function after stroke. *Am J Phys Med Rehabil*. 2012;91(11 Suppl 3):S242–S254.
- [14] Kadivar Z, Sullivan JL, Eng DP, et al. Robotic training and kinematic analysis of arm and hand after incomplete spinal cord injury: a case study. *IEEE Int Conf Rehabil Robot*. 2011;2011:5975429.
- [15] Edgerton VR, Roy RR. Robotic training and spinal cord plasticity. *Brain Res Bull*. 2009;78:4–12.
- [16] Prange GB, Jannink MJ, Groothuis-Oudshoorn CG, et al. Systematic review of the effect of robot-aided therapy on recovery of the hemiparetic arm after stroke. *J Rehabil Res Dev*. 2006;43:171–184.
- [17] Volpe BT, Krebs HI, Hogan N. Robot-aided sensorimotor training in stroke rehabilitation. *Adv Neurol*. 2003;92:429–433.
- [18] Lu EC, Wang RH, Hebert D, et al. The development of an upper limb stroke rehabilitation robot: identification of clinical practices and design requirements through a survey of therapists. *Disabil Rehabil Assist Technol*. 2011;6:420–431.
- [19] Kadivar Z, Sullivan JL, Eng DP, et al. RiceWrist robotic device for upper limb training: feasibility study and case report of two tetraplegic persons with spinal cord injury. *Int J Biol Eng*. 2012;2:27–38.
- [20] Pehlivan AU, Sergi F, Erwin A, et al. Design and validation of the RiceWrist-S exoskeleton for robotic rehabilitation after incomplete spinal cord injury. *Robotica*. 2014;32:1415–1431.
- [21] Dobkin BH. Motor rehabilitation after stroke, traumatic brain, and spinal cord injury: common denominators within recent clinical trials. *Curr Opin Neurol*. 2009;22:563–569.
- [22] Vanmulken DA, Spooren AI, Bongers HM, et al. Robot-assisted task-oriented upper extremity skill training in cervical spinal cord injury: a feasibility study. *Spinal Cord*. 2015;53:547–551.
- [23] Chang WH, Kim Y-H. Robot-assisted therapy in stroke rehabilitation. *J Stroke*. 2013;15:174–181.
- [24] Norouzi-Gheidari N, Archambault PS, Fung J. Effects of robot-assisted therapy on stroke rehabilitation in upper limbs: systematic review and meta-analysis of the literature. *J Rehabil Res Dev*. 2012;49:479–496.
- [25] Mehrholz J, Hadrich A, Platz T, et al. 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.
- [26] Veerbeek JM, Langbroek-Amersfoort AC, van Wgen EE, et al. Effects of robot-assisted therapy for the upper limb after stroke. *Neurorehabil Neural Repair*. 2017;31:107–121.
- [27] Celik B. Robotic technology for spinal cord injury: upper extremity [Turkish]. *Turk J Phys Med Rehab*. 2015;61:S32–S36.
- [28] Elwy AR, Groessl EJ, Eisen SV, et al. A systematic scoping review of yoga intervention components and study quality. *Am J Prev Med*. 2014;47:220–232.
- [29] King K, Meader N, Wright K, et al. Characteristics of interventions targeting multiple lifestyle risk behaviours in adult populations: a systematic scoping review. *PLoS One*. 2015;10:e0117015.
- [30] Moher D, Liberati A, Tetzlaff J, The PRISMA Group, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6:e1000097.
- [31] The Joanna Briggs Institute Reviewers' Manual 2015 Methodology for JBI Scoping Reviews [Internet]. Adelaide: Joanna Briggs; 2015 [cited 2017 Jun 22]. Available from: https://joannabriggs.org/assets/docs/sumari/Reviewers-Manual_Methodology-for-JBI-Scoping-Reviews_2015_v2.pdf
- [32] Chambers D, Rodgers M, Woolacott N. Not only randomized controlled trials, but also case series should be considered in systematic reviews of rapidly developing technologies. *J Clin Epidemiol*. 2009;62:1253–1260.
- [33] Peinemann F, Tushabe DA, Kleijnen J. Using multiple types of studies in systematic reviews of health care interventions – a systematic review. *PLoS One*. 2013;8:e85035.
- [34] Covidence [Internet]. Melbourne: Covidence; 2017 [cited 2017 Feb 13]. Available from: <https://www.covidence.org/>
- [35] Eng JJ, Teasell R, Miller WC, et al. Spinal cord injury rehabilitation evidence: method of the SCIRE systematic review. *Top Spinal Cord Inj Rehabil*. 2007;13:1–10.
- [36] National Collaborating Centre for Methods and Tools. [Internet]. Hamilton: McMaster University; 2010 [cited 2017 Feb 13]. Available from: <http://www.nccmt.ca/resources/search/9>
- [37] Saunders LD, Soomro GM, Buckingham J, et al. Assessing the methodological quality of nonrandomized intervention studies. *West J Nurs Res*. 2003;25:223–237.
- [38] Silverman SR, Schertz LA, Yuen HK, et al. Systematic review of the methodological quality and outcome measures utilized in exercise interventions for adults with spinal cord injury. *Spinal Cord*. 2012;50:718–727.
- [39] Teasell R, Bayona N, Marshall S, et al. A systematic review of the rehabilitation of moderate to severe acquired brain injuries. *Brain Injury*. 2007;21:107–112.
- [40] Methajarunon P, Eitvupart C, Diver CJ, et al. Systematic review of published studies on aquatic exercise for balance in patients with multiple sclerosis, Parkinson's disease, and hemiplegia. *Hong Kong Physiother J*. 2016;35:12–20.
- [41] World Health Organization [Internet]. Geneva: World Health Organization; 2017 [cited 13 Feb 2017]. Available from: <http://www.who.int/classifications/icf/en/>
- [42] Yozbatiran N, Keser Z, Davis M, et al. Transcranial direct current stimulation (tDCS) of the primary motor cortex and robot-assisted arm training in chronic incomplete cervical spinal cord injury: a proof of concept sham-randomized clinical study. *NeuroRehabil*. 2016;39:401–411.

- [43] Zariffa J, Kapadia N, Kramer JLK, et al. Feasibility and efficacy of upper limb robotic rehabilitation in a subacute cervical spinal cord injury population. *Spinal Cord*. 2012; 50:220–226.
- [44] Sledziewski L, Schaaf RC, Mount J. Use of robotics in spinal cord injury: a case report. *Am J Occup Ther*. 2012;66:51–58.
- [45] Yozbatiran N, Berliner J, Boake C, et al. Robotic training and clinical assessment of forearm and wrist movements after incomplete spinal cord injury: a case study. *IEEE Int Conf Rehabil Robot*. 2011;2011:5975425
- [46] Yozbatiran N, Berliner J, O'Malley M, et al. Robotic training and clinical assessment of upper extremity movements after spinal cord injury: a single case report. *J Rehabil Med*. 2012;44:186–188.
- [47] Cortes M, Elder J, Rykman A, et al. Improved motor performance in chronic spinal cord injury following upper-limb robotic training. *NeuroRehabil*. 2013;33:57–65.
- [48] Hoei T, Kawahira K, Fukuda H, et al. Use of an arm weight-bearing combined with upper-limb reaching apparatus to facilitate motor paralysis recovery in an incomplete spinal cord injury patient: a single case report. *J Phys Ther Sci*. 2017;29:176–180.
- [49] Frullo JM, Elinger J, Pehlivan AU, et al. Effects of assist-as-needed upper extremity robotic therapy after incomplete spinal cord injury: a parallel-group controlled trial. *Front Neurobot*. 2017;11:1–18.
- [50] Fitle KD, Pehlivan AU, O'Malley MK. A robotic exoskeleton for rehabilitation and assessment of the upper limb following incomplete spinal cord injury. *IEEE Int Conf Rehabil Robot*. 2015;4960–4966.
- [51] Chen YP, Howard AM. Effects of robotic therapy on upper-extremity function in children with cerebral palsy: a systematic review. *Dev Neurorehabil*. 2016;19:64–71.
- [52] Sackett DL, Rosenberg WMC, Gray JAM, et al. Evidence based medicine: what it is and what it isn't. *BMJ*. 1996;312:71–72.
- [53] Andrews K. The limitations of randomized controlled trials in rehabilitation research. *Clin Rehabil*. 1991;5:5–8.
- [54] Lancaster GA, Dodd S, Williamson PR. Design and analysis of pilot studies: recommendations for good practice. *J Eval Clin Pract*. 2004;10:307–312.
- [55] Anderson GL, Prentice RL. Individually randomized intervention trials for prevention and control. *Stat Methods Med Res*. 1999;8:287–309.
- [56] Lesko LJ, Zineh I, Huang SM. What is clinical utility and why should we care? *Clin Pharmacol Ther*. 2010;88: 729–733.
- [57] Iosa M, Morone G, Cherubini A, et al. The three laws of neurorobotics: a review on what neurorehabilitation robots should do for patients and clinicians. *J Med Biol Eng*. 2016;36:1–11.
- [58] Colombo R, Pisano F, Mazzone A, et al. Design strategies to improve patient motivation during robot-aided rehabilitation. *J Neuroeng Rehabil*. 2007;4:3.
- [59] Dijkers MP, deBear PC, Erlandson RF, et al. Patient and staff acceptance of robotic technology in occupational therapy: a pilot study. *J Rehabil Res Dev*. 1991;28:33–44.
- [60] Reinkensmeyer DJ, Dietz V. *Neurorehabilitation technology*. 2nd ed. California (LA): Springer International Publishing; 2016.
- [61] Norman DA, Draper SW. *User-centered system design: new perspectives on human-computer interaction*. Hillsdale: CBC Press; 1986.
- [62] Dobkin BH. Training and exercise to drive poststroke recovery. *Nat Clin Pract Neurol*. 2008;4:76–85.
- [63] Dobkin BH, Apple D, Barbeau H, et al. Weight-supported treadmill vs. over-ground training for walking after acute incomplete SCI. *Neurology*. 2006;66:484–493.
- [64] Winchester P, Smith P, Foreman N, et al. A prediction model for determining over ground walking speed after locomotor training in persons with motor incomplete spinal cord injury. *J Spinal Cord Med*. 2009;32:63–71.
- [65] Harkema S, Gerasimenko Y, Hodes J, et al. Effect of epidural stimulation of the lumbosacral spinal cord on voluntary movement, standing, and assisted stepping after motor complete paraplegia: a case study. *Lancet*. 2011;377: 1938–1947.
- [66] Fawcett JW, Curt A, Steeves JD, et al. Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: spontaneous recovery after spinal cord injury and statistical power needed for therapeutic clinical trials. *Spinal Cord*. 2007;45:190–205.
- [67] Ditunno JF, Stover SL, Freed MM, et al. Motor recovery of the upper extremities in traumatic quadriplegia: a multicenter study. *Arch Phys Med Rehabil*. 1992;73:431–436.
- [68] CIHR [Internet]. Canada (Ottawa):Donna Ciliska; 2012 [cited 2017 Jun 22]. Available from: <http://www.cihr-irsc.gc.ca/e/45235.html>
- [69] Fouad K, Krajacic A, Tetzlaff W. Spinal cord injury and plasticity: opportunities and challenges. *Brain Res Bull*. 2011;84:337–342.
- [70] Dietz V, Curt A. Neurological aspects of spinal-cord repair: promises and challenges. *Lancet Neurology*. 2006;5: 688–694.
- [71] Field-Fote EC. *Spinal cord injury rehabilitation*. Philadelphia: F. A. Davis Company; 2009.
- [72] Jakob W, Wirz M, van Hedel HJ, et al. Difficulty of elderly spinal cord injured subjects to translate motor recovery—body function - into activity of daily living. *J Neurotrauma*. 2009;26:2037–2044.
- [73] Failli V, Kopp MA, Gericke C, et al. Functional neurological recovery after spinal cord injury is impaired in patients with infections. *Brain*. 2012;135:3238–3250.
- [74] Maynard FM, Karunas RS, Waring WP. Epidemiology of spasticity following traumatic spinal cord injury. *Arch Phys Med Rehabil*. 1990;71:566–569.
- [75] Sie IH, Waters RL, Adkins RH, et al. Upper extremity pain in the postrehabilitation spinal cord injured patient. *Arch Phys Med Rehabil*. 1992;73:44–48.
- [76] Mulcahey MJ, Hutchinson D, Kozin S. Assessment of upper limb in tetraplegia: considerations in evaluation and outcomes research. *J Rehabil Res Dev*. 2007;44:91–102.
- [77] Pollock C, Freemantle N, Sheldon T, et al. Methodological difficulties in rehabilitation research. *Clin Rehabil*. 1993;7: 63–72.
- [78] Anderson K, Aito S, Atkins M, et al. Functional recovery measures for spinal cord injury: an evidence-based review for clinical practice and research. *J Spinal Cord Med*. 2008;31:133–144.
- [79] Zariffa J, Kapadia N, Kramer JLK, et al. Relationship between clinical assessments of function and measurements from an upper-limb robotic rehabilitation device in cervical spinal cord injury. *IEEE Trans Neural Syst Rehabil Eng*. 2012;20:341–350.
- [80] Elkins MR, Herbert RD, Moseley AM, et al. Rating the quality of trials in systematic reviews of physical therapy interventions. *Cardiopulm Phys Ther J*. 2010;21:20–26.

- [81] Kwan J, Sandercock P. In-hospital care pathways for stroke. *Cochrane Database Syst Rev.* 2003;34:587–588.
- [82] Friedman L. Commentary: why we should report results from clinical trial pilot studies. *Trials.* 2013;14:14–14.
- [83] The Cochrane Collaboration [Internet]. London: Cochrane; 2011 [cited 2017 Jun 22]. Available from: <http://training.cochrane.org/handbook>

Appendix 1. Full database searches.

The Medline search as follows: 1. Exp spinal cord injuries/ 2. Exp paraplegia/ 3. Exp quadriplegia/ 4. Spinal cord compression/ 5. (Spinal cord adj3 (injur* or contusion* or trauma* or transection* or laceration* or compression* or damag*)).tw,kw/ 6. (Myelopath* adj3 (traumatic or post-traumatic or post traumatic)).tw,kw/ 7. ((central cord injur* or central spinal cord) adj3 syndrome*).tw,kw/ 8. (paraplegi* or quadriplegi* or tetraplegi* or locked-in syndrome).tw,kw/ 9. Or/1–8/10. Robotics/ 11. Bionics/ 12. Automation/ 13. Exoskeleton Device/ 14. (Robot* or exoskelet* or telerobot* or wrist-robot*).tw,kw/ 15. Or/10–14/ 16. Exp upper extremity/ 17. (Upper* adj3 (limb* or extremi* or body)).tw,kw/ 18. (Upper-extremi* or upper-limb*).tw,kw/19. Or/16–18/ 20. 9 and 15 and 19/ 21. animals/not (animals/and humans/) 22. 20 not 21/ 23. Remove duplicates from 22.

The CCTR search as follows: 1. Exp spinal cord injuries/ 2. Exp paraplegia/ 3. Exp quadriplegia/ 4. Spinal cord compression/ 5. (Spinal cord adj3 (injur* or contusion* or trauma* or transection* or laceration* or compression* or damag*)).tw,kw/ 6. (Myelopath* adj3 (traumatic or post-traumatic or post traumatic)).tw,kw/ 7. ((Central cord injur* or central spinal cord) adj3 syndrome*).tw,kw/ 8. (Paraplegi* or quadriplegi* or tetraplegi* or locked-in syndrome).tw,kw/ 9. Or/1–8/ 10. Robotics/ 11. Bionics/ 12. Automation/ 13. Exoskeleton device/ 14. (Robot* or exoskelet* or telerobot* or wrist-robot*).tw,kw/ 15. or/10–14/ 16. Exp upper extremity/ 17. (Upper* adj3 (limb* or extremi* or body)).tw,kw/ 18. (Upper-extremi* or upper-limb*).tw,kw/ 19. Or/16–18/ 20. 9 and 15 and 19/ 21. animals/ not (animals/and humans/) 22. 20 not 21/ 23. Remove duplicates from 22.

The CDSR search as follows: 1. (Spinal cord adj3 (injur* or contusion* or trauma* or transection* or laceration* or compression* or damag*)).tw,kw. 2. (Myelopath* adj3 (traumatic or post-traumatic or post traumatic)).tw,kw. 3. ((central cord injur* or central spinal cord) adj3 syndrome*).tw,kw. 4. (Paraplegi* or quadriplegi* or tetraplegi* or locked-in syndrome).tw,kw. 5. Or/1–4. 6. (Robot* or exoskelet* or telerobot* or wrist-robot*).tw,kw. 7. 5 and 6 8. (upper* adj3 (limb* or extremi* or body)).tw,kw. 9. (Upper-extremi* or upper-limb*).tw,kw. 10. Or/8–9. 11. 7 and 10.

The CINAHL search as follows: S1. (MH "spinal cord injuries+") S2. (MH "paraplegia+") S3. (MH "quadriplegia") S4. TI (spinal cord N3 (injur* or contusion* or trauma* or transection* or laceration*

or compression* or damag*)) OR AB (spinal cord N3 (injur* or contusion* or trauma* or transection* or laceration* or compression* or damag*)) S5. TI (myelopath* N3 (traumatic or post-traumatic or post traumatic)) OR AB (myelopath* N3 (traumatic or post-traumatic or post traumatic)) S6. TI (central cord injur* or central spinal cord) N3 syndrome*) OR AB ((central cord injur* or central spinal cord) N3 syndrome*) S7. TI ((paraplegi* or quadriplegi* or tetraplegi* or locked-in syndrome)) OR AB ((paraplegi* or quadriplegi* or locked-in syndrome or tetraplegi*)) S8. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 S9. (MH "Robotics") S10. (MH "Bionics") S11. (MH "Automation") S12. TI ((robot* or exoskelet* or telerobot* or wrist-robot*)) OR AB ((robot* or exoskelet* or telerobot* or wrist-robot*)) S13. S9 OR S10 OR S11 OR S12 S14. (MH "upper extremity+") S15. TI (upper* N3 (limb* or extremi* or body)) OR AB (upper* N3 (limb* or extremi* or body)) S16. TI ((upper-extremi* or upper-limb*)) OR AB ((upper-extremi* or upper-limb*)) S17. S14 OR S15 OR S16 S18. S8 AND S13 AND S17.

The Embase search as follows: 1. Exp spinal cord injury/ 2. Exp paraplegia/ 3. Exp quadriplegia/ 4. (Spinal cord adj3 (injur* or contusion* or trauma* or transection* or laceration* or compression* or damag*)).tw,kw/ 5. (myelopath* adj3 (traumatic or post-traumatic or post traumatic)).tw,kw/ 6. ((central cord injur* or central spinal cord) adj3 syndrome*).tw,kw/7. (Paraplegi* or quadriplegi* or tetraplegi* or locked-in syndrome).tw,kw/ 8. Or/1–7/ 9. Robotics/ 10. Bionics/ 11. Automation/ 12. Exp "exoskeleton (rehabilitation)"/ 13. (Robot* or exoskelet* or telerobot* or wrist-robot*).tw,kw/ 14. Or/9–13/ 15. Exp upper limb/ 16. (Upper* adj3 (limb* or extremi* or body)).tw,kw/ 17. (Upper-extremi* or upper-limb*).tw,kw/ 18. Or/15–17/ 19. 8 and 14 and 18/ 20. (Exp animals/ or exp animal experimentation/ or nonhuman/) not ((exp animals/or exp animal experimentation/ or nonhuman/) and exp human/) 21. 19 not 20/ 22. Journal: conference abstract.pt/ 23. 21 not 22/ 24. Remove duplicates from 23.

The PsycINFO search as follows: 1. Spinal cord injuries/ 2. Paraplegia/ 3. Quadriplegia/ 4. (Spinal cord adj3 (injur* or contusion* or trauma* or transection* or laceration* or compression* or damag*)).tw,kw/ 5. (Myelopath* adj3 (traumatic or post-traumatic or post traumatic)).tw,kw/ 6. ((Central cord injur* or central spinal cord) adj3 syndrome*).tw,kw. 7. (Paraplegi* or quadriplegi* or tetraplegi* or locked-in syndrome).tw,kw/ 8. Or/1–7/ 9. Robotics/ 10. (Robot* or exoskelet* or telerobot* or wrist-robot*).tw,kw/ 11. 9 or 10/ 12. "Arm (anatomy)"/ 13. "Fingers (anatomy)"/ 14. "Hand (anatomy)"/ 15. "Elbow (anatomy)"/ 16. "Shoulder (anatomy)"/ 17. Wrist/ 18. (Upper* adj3 (limb* or extremi* or body)).tw,kw. 19. (Upper-extremi* or upper-limb*).tw,kw. 20. Or/12–19/ 21. 8 and 11 and 20/ 22. Limit 21 to human.