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Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

The influence of training volume in rehabilitation with robotic devices for patients with cervical spinal cord injuries: a systematic review

Eline Bollen
Hanne Rombaut

Eerste deel van het scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie

PROMOTOR :

Prof. dr. Annemie SPOOREN

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‘The influence of training volume in rehabilitation with robotic devices for patients with cervical spinal cord injuries: a systematic review’

Research question

What is the influence of training volume during the rehabilitation of chronic, incomplete cervical spinal cord injuries, with the use of robotic devices, on functioning?

Highlights

- The research on robotic rehabilitation in patients with chronic, incomplete cervical spinal cord injuries is limited. The research that is available is of moderate to low quality.
- There is no consensus on the training volume for this population. The included studies show a wide range of frequency, session duration, number of repetitions, and intensity.
- The findings of this literature review suggest that a robotic rehabilitation program improves muscle strength and functionality of the hand or arm, although not all studies could support their reported improvements with statistically significant values. In most studies, functional improvements did not result in higher independence of the participants.

Bollen Eline and Rombaut Hanne

1st Master 2020-2021

Promotor: Prof. dr. SPOOREN Annemie

Context of the master thesis

The aim of this master thesis is to research the influence of the training volume in rehabilitation with the use of robotics on arm and hand function in patients with chronic, incomplete cervical spinal cord injuries (SCI).

The thesis is situated in the domain of neurological rehabilitation, since it includes patients with chronic, incomplete cervical spinal cord injuries. The term training volume is a term that is also used in the domain of musculoskeletal rehabilitation and cardio-respiratory rehabilitation.

The worldwide cases of spinal cord injuries range from 13.1 to 163.4 per million people in developed countries around the world. Of the spinal cord, the cervical spine is the area that is most damaged in the cases. The technology of training with robotics for the rehabilitation of cervical SCI is rather new. Based on research we can cautiously conclude that it shows potential. This master thesis might be relevant for all therapists who are active in the abovementioned domain and population and who are searching for a new manner of rehabilitation that can potentially be the next step for technology used in rehabilitation.

The first part of this master thesis, the literature review, is a stand-alone project and is not part of another investigation. It takes place at Hasselt University in Diepenbeek. The second part, the research protocol, is likewise not part of another investigation. The place of this will be determined in the future. Presumably, it will take place in a single center rehabilitation facility in the vicinity of Hasselt University.

A central format was used for this duo master thesis.

For this master thesis, the research question was provided by the students and thereafter adapted and approved by the promotor. The research methodology was determined by the students based on introductory literature. This literature was the result of an introductory search on the domain being investigated. After approval of the promoter, the articles were screened independently by both students. The data-extraction was performed by one of the students and quality assessment was performed independently by both students. This

master thesis was a result of an equal contribution of both students. All steps were consulted with the promoter and approved by the promoter.

Lastly, the research protocol was the final part of this master thesis. The protocol was written by both students, who contributed equally. The different topic sections were adapted based on the feedback and later approved by the promoter.

Part 1: literature search

1. Abstract

Background: Robotic rehabilitation has been proven to be effective for stroke patients. Most research regarding robotics is for the rehabilitation of the lower extremity (e.g., gait training). Because of the rather new intervention on robotics, there is no consensus regarding training volume (session duration, intensity, repetitions…).

Methods: A systematic literature search was conducted to evaluate the evidence available for rehabilitation programs regarding the upper extremity with the use of robotics for patients with chronic, incomplete cervical spinal cord injuries.

Results: A robotic rehabilitation program improves muscle strength and functionality of the hand or arm, although not all studies could support their reported improvements with statistically significant values. In most studies, functional improvements did not result in higher independence of the participants.

Discussion and conclusion: The quality of the included studies is low because of the limited available research. Therefore, the results of this study should be interpreted with care.

Aim of the study: This review will research the influence of the training volume in rehabilitation with the use of robotics on arm and hand function in patients with chronic, incomplete cervical SCI.

Research question: What is the influence of training volume during the rehabilitation of chronic, incomplete cervical SCI, with the use of robotic devices, on functioning?

Key words: robotics, exoskeleton, end-effector, cervical SCI, training volume

2. Introduction

The spinal cord transports signals, either sensory or motor information, from muscles and organs to the brain and vice versa. Damage to the spinal cord disrupts this transport and leads to tetra- or quadriplegia with impairments in the upper extremities, trunk and/or lower extremities, depending on the level of injury. Worldwide, the leading causes of SCI are vehicle accidents and falls. The incidence and prevalence of SCI have increased over time, in part because of the increase in human activity. It ranges from 13.1 to 163.4 per million people in developed countries around the world. The area that was most injured was the cervical spine. Traumatic SCI is most likely to result in complete injuries (ASIA A or B). In contrast, non-traumatic injuries often result in incomplete SCI (ASIA C or D). Spinal cord injuries lead to death in 3.1% to 22.2% of the cases. The people that are more prevalent to have an SCI are males with ages ranging from 14.6 to 67.6 years (Kang et al., 2017).

In clinical practice, physiotherapists use an international classification tool known as the American Spinal Injury Association (ASIA) scale. This is used to help determine which levels of the spinal cord are damaged and which levels are completely or partially intact. It is a classification based on the amount of damage to the spinal cord: complete and incomplete lesions. Someone with an incomplete injury might still maintain some sensory and/or motor function below the neurological level. Whereas with a complete injury, there is no sensory and/or motor function left. The scale also has a classification based on degree of impairment, using the letters A through E, where A is a complete loss of function and E is normal function (Kirshblum et al., 2011).

The study from Anderson (2004) determined what areas of functional recovery the SCI population would most like researchers to address to have a positive effect on their quality of life. They concluded that the return of arm and hand function was the highest priority for quadriplegics. Sexual function was the highest priority for paraplegic patients. Regaining bladder and bowel control was also an important factor. Furthermore, all SCI participants from the study regarded exercise as a priority to their functional recovery.

Training volume can be defined as a combination of training frequency, duration, amount, and intensity. The training amount can be altered by changing the number of repetitions and actual therapy time. In addition to repetitions, intensity of training can be increased by

adding a greater load or by evolving to a more difficult movement (Lang, Lohse, & Birkenmeier, 2015; Zbogar, Eng, Miller, Krassioukov, & Verrier, 2017).

The systematic review of X. Lu, Battistuzzo, Zoghi, & Galea (2015) reports that training can improve arm and hand function in people with cervical SCI, both in acute and chronic phases of their recovery. Even if training is initiated in the chronic phase, improvements in arm and hand function, muscle strength, and quality of life are achieved through training. For this reason, chronic SCI patients should be stimulated to take part in physical rehabilitation interventions. The focus of these interventions should be on improving arm and hand function as this is a priority for this population.

The use of robotic devices has been shown to be effective in therapy for upper limb rehabilitation in stroke patients (Janne M. Veerbeek, Langbroek-Amersfoort, Van Wegen, Meskers, & Kwakkel, 2017). However, for other neurological injuries, the evidence has been limited. 'A key feature of robotics devices used for neurological rehabilitation is that the device can be used for assessment of motor impairment in addition to its primary function of delivering high intensity-controlled therapy' (Fitle, Pehlivan, & O'Malley, 2015).

Robotic devices can be divided into two main categories, exoskeletons, and end-effectors. An exoskeleton is a wearable device with several joints conforming to human anatomy, for example the ArmeoPower, IntelliArm, and EXO-UL7. When patient-device contact is only at the end-effector position, then the devices are end-effectors. Some examples of these are the MIT-MANUS, Assisted Rehabilitation and Measurement Guide, and the Bi-Manu-Track (Nuray Yozbatiran & Francisco, 2019).

The research on robotic rehabilitation is extensive for lower extremity training, regarding gait rehabilitation. However, for upper limb rehabilitation the research is limited and mainly focusing on the stroke population (Nuray Yozbatiran & Francisco, 2019). There were two major systematic reviews performed, the review of Yozbatiran and Francisco (2019) and the one of Singh et al. (2018). Yozbatiran and Francisco (2019) reported a review on robotic rehabilitation in the SCI population. The researchers included all studies where a robotic device was used to improve arm and function. No further specification was made based on the recovery stage (acute, subacute, chronic) and type of injury (complete, incomplete). Thus, the review included patients in the subacute and chronic stage of recovery and both

with complete and incomplete injuries. The training volume varied in the included studies for the duration of the treatment program (two weeks to six weeks), frequency (one day/week to five days/week), and session duration (20 minutes to 180 minutes). The researchers found that the efficacy of robot-assisted training for arm and hand function and independence in daily life seems positive. The review reported improvements in muscle strength, active range of motion, arm and hand function, and pinch and grip strength. These results need to be interpreted with caution because of the sparse number of included studies.

Similarly, the review of Singh et al. (2018) chose a broad aim for the review. The researchers wanted to determine the effectiveness and feasibility of robotic-assisted interventions in upper extremity (UE) rehabilitation programs for individuals with tetraplegia, to describe the characteristics of the participants, what robotic training protocols have been employed to restore motor function and to highlight considerations for future studies. The researchers used a non-specific search-strategy. Namely, all studies were included if an intervention with a robotic device to assist UE training in tetraplegia patients due to cervical SCI (traumatic or non-traumatic) was performed. Participants in the subacute and chronic recovery stage were listed. The RiceWrist, RiceWrist-S, MAHI EXO-II, Haptic Master, InMotion 3.0 Wrist Robot, ArmeoSpring, ReoGo, and the Reaching Robot were used as the robotic device in the interventions. These earlier-mentioned devices were classified by the authors as exoskeletons and end-effectors. Overall, the training protocols varied in intervention length (two weeks to six weeks) and duration of the session (40 minutes to three hours). This review concluded that the use of robots for UE SCI rehabilitation appears to be feasible and has some beneficial utility. However, the effectiveness of robotic training was inconclusive, which highlights the need for further research with larger sample sizes to develop effective training protocols. Lastly, Singh et al. (2018) reported four knowledge gaps, being clinical utility of robotic devices, optimal training protocols, optimal participants, and appropriateness of outcome measures.

To this day, there is no consensus of what the training volume should be when rehabilitation with different types of robotics is used. Some studies, considering the SCI population, stand by a long duration of activity training the robotics (Eng et al., 2011; Francisco et al., 2017; Pehlivan et al., 2014), some studies do not specify their training volume (Krebs et al., 2008;

Osuagwu et al., 2020) and others report a smaller training volume (Hwan Jung et al., 2019; Shimizu et al., 2017). For this reason, we conducted this review in the hope that the first step to a consensus on training volume for robotic rehabilitation can be made.

The reviews of Yozbatiran and Francisco (2019) and Singh et al. (2018) did not specify the research population based on the stage of recovery and form of injury. The researchers of the abovementioned reviews also did not research the effect of dosage of the training intervention. Singh et al. (2018) did not perform a literature search with a specific search strategy. The review of Yozbatiran and Francisco (2019) did not have a clearly defined aim for the study, thus it is classified as a review and not a systematic review. For these reasons, this systematic review will research the influence of the training volume in rehabilitation with the use of robotics on arm and hand function in patients with a chronic, incomplete cervical SCI. We hypothesized that if the training volume increases, the arm and hand function should increase similarly.

3. Methods

3.1 Research question

What is the influence of training volume during the rehabilitation of chronic, incomplete cervical SCI, with the use of robotic devices, on functioning?

3.2 Literature search

A systematic literature search was conducted on Pubmed, Web of Science, Elsevier, and Scopus. The MESH terms ‘spinal cord injuries’, ‘robotics’, and ‘upper extremity’ were used with the Boolean operator AND. ‘Stroke’ and ‘lower extremity’ were used with the NOT operator to exclude those topics from the search. The last search term used was ‘exoskeleton device’ to incorporate the use of exoskeletons and robotics in the review.

Study Designs

A challenge that arose for this study was the limited amount of evidence on this topic. Therefore, no form of study was excluded from this review. We included randomized controlled trials (RCT), pilot RCTs, case reports, case series, case studies, and pilot studies.

3.3 Selection criteria

We included all studies examining the human population with chronic cervical SCIs with a classification C or D on the ASIA scale (Roberts et al., 2016). Studies were also included if they examined an intervention on upper extremity training and if they used some sort of robotics and/or exoskeleton for that intervention. At last, primarily English written studies were enclosed.

Studies that researched the use of robotics for the lower extremities or any other form of rehabilitation method for the lower extremities were excluded from this systematic review. If studies involved participants with SCI in any other place than the cervical spine, they were excluded as well.

Interventions

Intervention programs consist of active movement training with a robotic device, preferably not in combination with another kind of intervention. No selection was made on the characteristics of the robotic device. Robotic training could be done with analytical movements, in the form of games or task-hitting exercises or a combination of both.

Outcomes

This review is interested in gains in functionality, therefore attention was given to functional outcomes during screening. The use of outcome measures such as muscle strength, grip/pinch strength, capability to perform ADL activities, level of independence, etc. was necessary to be included in this study.

3.4 Quality assessment

Quality assessment was performed in two phases. The first phase of assessment was done with the PEDRO-tool. To further assess the quality of the case reports, a second assessment was performed on studies with scores lower than six on the PEDRO-tool. This assessment was done with the STROBE-checklist (Cochrane Collaboration, 2021).

Both assessments were performed independently by both reviewers and compared later on. Discrepancies were discussed and finalized.

3.5 Data-extraction

Following data were extracted from the included studies: study design, study objective, number of participants, sex and age of the participants, ASIA-scores and level of SCI, time since injury, type of robot and trained movements, trained side, assessment times, intervention protocol, assessed outcomes, results and conclusion of the study.

4. Results

4.1 Study selection

The study selection was done by two independent researchers (EB, HR). Selection started with 128 studies, of which 28 duplicates were removed. One hundred articles were screened for title and abstract, this led to the exclusion of 68 studies that did not meet our criteria. Thereafter the remaining 26 articles were assessed for full-text eligibility. Fourteen articles were removed. Seven articles had the wrong intervention, in three the patient population was wrong, three studies had the wrong study design and lastly one had the wrong outcome. Ultimately our systematic review includes 12 studies (Figure 1).

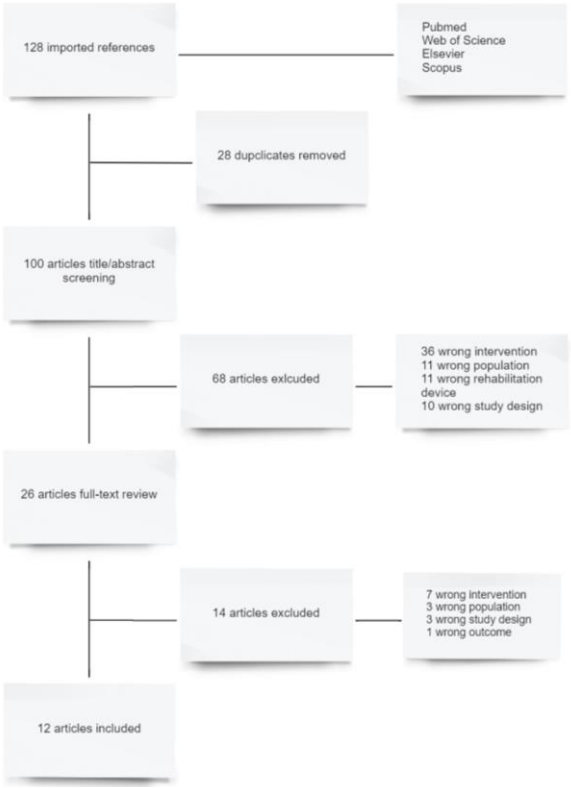


Figure 1: Study selection

4.2 Quality assessment

Of these 12 included studies, two were RCT's while the remaining ten were pilot studies and/or case reports. Results are shown in Table *1*. Since only two studies were RCT's, the overall scores on the PEDRO were low. Results of the second assessment with the STROBE-checklist are shown on Table *2*. Overall scores after a second assessment remained low. Analyses of the results showed that assessment points were lost most frequently on items such as the use of statistical analyses methods, acknowledgment of study limitations, effort to control bias etc. Low scores on quality assessment were expected, given the scarce availability of scientifically strong studies on the subject, such as RCT's. In this light, no studies were excluded after quality assessment.

4.3 Data-extraction

Study participants

A total of 119 participants were included in the studies, with a total of 15 dropouts. Of those 119, 88 were male and 22 females. Mean age of all the participants was 38,6 years. The mean time since injury was 63,3 months. ASIA scores ranged from A to D, though most participants had scores C or D. Level of injury was widely spread, ranging from C2 to C8.

Table 1: Scoring PEDRO

	(Cortes et al., 2013)	**(Francisco et al., 2017)**	**(Eng et al., 2011)**	**(Hwan Jung et al., 2019)**	**(Kim et al., 2019)(Hwan Jung et al., 2019)**	**(Osuagwu et al., 2020)**	**(Pehlivan et al., 2014)**	(Z. Lu et al., 2017)	**(Shimizu et al., 2017)**	(Vanmulken et al., 2015)	**(N. Yozbatiran et al., 2011)**	**(Nuray Yozbatiran et al., 2012)**
1. Eligibilty criteria	1	1	0	1	1	1	0	0	0	1	1	0
2. Random allocation	0	0	0	1	1	0	0	0	0	0	0	0
3. Concealed allocation	0	0	0	0	1	0	0	0	0	0	0	0
4. Similarity group at baseline	0	0	0	0	1	1	0	0	0	0	0	0
5. Subject blinding	0	0	0	0	0	0	0	0	0	0	0	0
6. Therapist blinding	0	0	0	0	0	0	0	0	0	0	0	0
7. Assessors blinding	0	0	0	0	1	0	0	0	0	0	0	0
8. Measurements 85% of subjects	1	0	1	0	1	0	1	1	1	0	1	1
9. Allocated treatment	1	1	1	1	1	1	1	1	1	1	1	1
10. Reported results	0	0	1	1	1	0	0	0	0	0	0	0
11. point measure/measure of variability	0	1	0	1	1	1	1	0	0	0	0	0
TOTAL	3	3	3	5	9	4	3	2	2	2	3	2

Table 2: Scoring STROBE

	(Cortes et al., 2013)	(Francisco et al., 2017)	(Eng et al., 2011)	(Hwan Jung et al., 2019)	(Kim et al., 2019)(Hwan Jung et al., 2019)	(Osuagwu et al., 2020)	(Pehlivan et al., 2014)	(Z. Lu et al., 2017)	(Shimizu et al., 2017)
1a	0	1	1	0	1	1	1	1	1
1b	1	1	1	1	1	1	1	1	1
2	1	1	1	1	1	1	1	1	1
3	1	1	1	1	1	1	1	1	1
4	1	1	1	1	1	1	1	1	1
5	1	1	1	1	1	1	1	1	1
6	1	1	1	1	1	1	1	1	1
6b	/	/	/	/	/	/	/	/	/
7	1	1	1	1	1	1	1	1	1
8	1	1	1	1	1	1	0	1	0
9	0	0	0	0	0	0	0	0	0
10	1	1	0	1	1	0	0	0	1
11	1	0	1	1	1	0	0	0	0
12a	1	1	0	1	1	1	0	0	0
12b	1	0	0	1	0	1	0	0	0
12c	/	/	/	/	/	/	/	/	/
12d	/	/	/	/	/	/	/	/	/
12	0	0	0	0	0	0	0	0	0
13a	1	1	1	1	1	1	1	1	1
13b	1	1	0	1	1	0	0	0	1
13c.	0	0	0	1	1	0	0	0	0
14a	1	1	1	1	1	1	1	1	1
14b	1	1	0	0	1	0	0	0	0
15	/	/	/	/	/	/	/	/	/
16a	/	/	/	/	/	/	/	/	/
16b	/	/	/	/	/	/	/	/	/
17	0	0	0	0	0	1	0	0	0
18	1	1	1	1	1	1	1	1	1
19	1	0	0	1	1	0	0	0	0
20	1	1	1	1	1	1	1	1	1
21.	1	0	0	0	1	0	0	0	0
22	0	0	1	1	1	1	0	1	0
TOTAL	20	17	15	20	22	17	12	14	14

Interventions

Robotic devices and trained movements

Throughout the included studies, a variety of robotics were used. Each robotic device has its own characteristic, e.g., more proximal, or distal devices, functional movements or specific activities. Table *3* gives an overview of the robotic characteristics used in the included studies. Almost all studies used exoskeleton robotics such as the InMotion Wrist Robot (Cortes et al., 2013), RiceWrist (Eng et al., 2011; N. Yozbatiran et al., 2011), Hand of Hope (Z. Lu, Tong, Shin, Stampas, & Zhou, 2017), MAHI Exo-II (Francisco et al., 2017; Nuray Yozbatiran et al., 2012). Hwan Jung et al. (2019) used an exoskeleton (ArmeoPower) as well as an end-effector (Amadeo). Osuagwu et al. (2020) used a soft robotic glove, known as the SEM Glove. The glove is built with tendon-like structures alongside each finger that amplify the participants' produced force.

Movements performed with the robotic device differed depending on the primary focus of the device, meaning more proximal or more distal movements. The majority of the studies focused on distal movements, mostly training forearm, wrist and hand with movements such as flexion/extension of elbow and wrist, radial/ulnar deviation of the wrist and supination/pronation of the forearm (Cortes et al., 2013; Eng et al., 2011; Francisco et al., 2017; Kim et al., 2019; Nuray Yozbatiran et al., 2012). Lu et al.(2017) used the 'Hand of hope', which focused exclusively on hand movements such as hand closing/opening and opening/closing of individual fingers. Only Hwan Jung et al. (2019) and Kim et al. (2019)used the ArmeoPower, an exoskeleton that also includes training of the shoulder, with proximal movements such as abduction/adduction, flexion/extension, and internal/external rotation of the shoulder.

All robotic devices had different training modes that could be selected during a session: the passive, the active-assisted or triggered, and the active mode. In the passive mode the robotic device, as the name suggests, passively moves the participant's arm, no input from the participant is required. During active-assisted or triggered mode, the participant's movements are partially assisted, or it requires some initial input to initiate movement, to overcome a certain threshold before the robot takes over. In the active mode, participants move the arm themselves, frequently against a set amount of resistance. (Cortes et al.,

2013; Eng et al., 2011; Francisco et al., 2017; Hwan Jung et al., 2019; Vanmulken, Spooren, Bongers, & Seelen, 2015; N. Yozbatiran et al., 2011; Nuray Yozbatiran et al., 2012).

Although different robotics were used in the included studies, almost all interventions comprise the following elements: analytic, single joint movements of the arm and/or wrist, and a target hitting game. Vanmulken et al. (2015) used an intervention based on ADL activities such as eating with a fork and knife, taking money out of a purse, moving a cup, etc. Similarly, Osuagwu et al. (2020) used a home-based intervention with the SEM Glove where the participants exclusively performed ADL activities. In Hwan Jung et al. (2019), Kim et al. (2019) and Shimizu et al. (2017), robotics training was combined with conventional physical therapy.

Training intensity

For this review, information about the intensity of the intervention was very important. Training intensity consists of a combination of elements: duration of the intervention and each training session, frequency of the sessions, amount of repetitions during these sessions, and amount of resistance of movements (Lang et al., 2015). Overall, all studies mentioned the duration of their intervention, their session frequency, and their session duration. Information about the amount of movement repetitions was available only in the studies of Cortes et al. (2013), Francisco et al. (2017), Kim et al. (2019) and Yozbatiran et al. (2012) and even then it was not specific. Cortes et al. (2013) used a total number of 1000 repetitions per session, divided over different movements. In the study of Francisco et al. (2017), the number of repetitions gradually progressed from 200 on day one to approximately 1000-1500 repetitions on day twelve. Similarly, Yozbatiran et al. (2012) increased their total number of repetitions from 87 to 800 throughout their intervention. Other studies only mention that training intensity was progressed gradually by increasing the number of repetitions, amount of resistance from the robotic device and the amount of threshold force needed in the triggered mode (Eng et al., 2011; Z. Lu et al., 2017; N. Yozbatiran et al., 2011). Osuagwu et al. (2020) gave their participants individual ADL tasks with a minimum number of repetitions they needed to complete on a daily basis. Vanmulken et al. (2015), Shimizu et

al. (2017) and Hwan Jung et al. (2019) did not mention anything about the amount of repetitions.

The duration of treatment ranged from four (Francisco et al., 2017; Kim et al., 2019; N. Yozbatiran et al., 2011; Nuray Yozbatiran et al., 2012), six (Cortes et al., 2013; Vanmulken et al., 2015), ten (Z. Lu et al., 2017) or 12 weeks (Osuagwu et al., 2020; Shimizu et al., 2017). Session frequency ranged from three or four times a week to daily sessions on consecutive weekdays. Session duration differed from 30-50 minutes (Hwan Jung et al., 2019; Kim et al., 2019; Shimizu et al., 2017) to three/four hours (Eng et al., 2011; Francisco et al., 2017; Osuagwu et al., 2020; N. Yozbatiran et al., 2011; Nuray Yozbatiran et al., 2012). Overall, the total amount of hours spent training with a robotic device ranged from eight (Shimizu et al., 2017) to 40 hours (Z. Lu et al., 2017). A more detailed summary of the intervention characteristics is presented in Table *4*.

Table 3: Robot characteristics

Study	Used robotic	Exoskeleton/End-effector	Trained movements
(Cortes et al., 2013)	InMotion 3.0 Wrist Robot	Exoskeleton	Wrist (flexion/extension, radial/ulnar deviation) and forearm (pronation/supination)
(Eng et al., 2011)	RiceWrist	Exoskeleton	Wrist (flexion/extension, radial/ulnar deviation) and forearm (pronation/supination)
(Francisco et al., 2017)	MAHI Exo-II	Exoskeleton	Elbow, forearm and wrist (no further specifics given)
(Hwan Jung et al., 2019)	ArmeoPower Amadeo	Exoskeleton End-effector	Shoulder (flexion/extension, AB/AD, internal/external rotation), elbow (flexion/extension), forearm (pronation/supination) and wrist (flexion/extension) Hand and fingers (3rd distal interphalangeal flexion and 5th finger abduction)
(Kim et al., 2019)	ArmeoPower	Exoskeleton	Shoulder (flexion/extension, AB/AD, internal/external rotation), elbow (flexion/extension), forearm (pronation/supination) and wrist (flexion/extension)
(Pehlivan et al., 2014)	RiceWrist	Exoskeleton	Wrist (target hitting)
(Osuagwu et al., 2020)	SEMGlove	Bionic glove, sensors that strengthen users own force	Hand and fingers (ADL training)
(Z. Lu et al., 2017)	Hand of Hope	Exoskeleton	Hand (closing/opening) and fingers (opening/closing)
(Shimizu et al., 2017)	Hybrid Assistive Limb (HAL)	Exoskeleton	Elbow (flexion/extension)
(Vanmulken et al., 2015)	Haptic Master		Distal part of forearm (ADL training)
(N. Yozbatiran et al., 2011)	RiceWrist	Exoskeleton	Wrist (flexion/extension, radial/ulnar deviation) and forearm (pronation/supination)
(Nuray Yozbatiran et al., 2012)	MAHI Exo-II	Exoskeleton	Elbow (flexion/extension), forearm (supination/pronation) and wrist (flexion/extension, radial/ulnar deviation)

Table 4: Overview interventions

Study and study design		Robotic device	Trained side	Trained movements	Intervention program		
					Frequency and duration	Total training hours	# repetitions
(Cortes et al., 2013)	Pilot study	InMotion3.0 Wrist Robot	Right side (dominant side)	Joint movement: wrist flexion/extension, radial/ulnar deviation and pronation/supination	(Cortes et al., 2013)	Pilot study	InMotion3.0 Wrist Robot
(Eng et al., 2011)	Case study	RiceWrist	Both sides	Joint movements: wrist flexion/extension, radial/ulnar deviation, forearm pronation/supination Target hitting task through a game	(Eng et al., 2011)	Case study	RiceWrist
(Francisco et al., 2017)	Pilot study	MAHI Exo-II	Both sides	Joint movements: elbow, forearm and wrist (no further specifics)	(Francisco et al., 2017)	Pilot study	MAHI Exo-II
(Hwan Jung et al., 2019)	RCT	ArmeoPower and Amadeo	Side that scored lowest on UEMS	Joint movements: elbow flexion/extension, wrist extension, 3rd distal interphalangeal flexion and 5th finger abduction. Movements trained if forms of game.	(Hwan Jung et al., 2019)	RCT	ArmeoPower and Amadeo
(Kim et al., 2019)	RCT	ArmeoPower	Side that scored lowest on UEMS	Joint movements: shoulder flexion/extension, AB/AD, internal/external rotation. Elbow flexion/extension. Forearm pronation/supination. Wrist flexion/extension	(Kim et al., 2019)	RCT	ArmeoPower
(Pehlivan et al., 2014)	Case study	SEMGlove	Participants chose themselves	Home based functional training: ADL tasks such as grasping and releasing, using cutlery, writing….	(Pehlivan et al., 2014)	Case study	SEMGlove
(Osuagwu et al., 2020)	Pilot study	RiceWrist	Left side	Target hitting tasks with changing level of resistance.	(Osuagwu et al., 2020)	Pilot study	RiceWrist
(Z. Lu et al., 2017)	Case study	Hand of hope	Right hand (dominant side)	Joint movements: hand closing/opening. Thumb, index finger and middle finger closing/opening. Middle, ring, and little fingers closing/opening	(Z. Lu et al., 2017)	Case study	Hand of hope
(Shimizu et al., 2017)	Case study	Hybrid Assistive Limb (HAL)	Both sides	RT: single joint movement of elbow flexion/extension	(Shimizu et al., 2017)	Case study	Hybrid Assistive Limb (HAL)

(Vanmulken et al., 2015)	Multiple case study	Haptic Master (HM)	Participants chose themselves, mostly side with poorest hand function	ADL activities chosen such as eating with fork and knife, taking money out of purse, moving a cup	(Vanmulken et al., 2015)	Multiple case study	Haptic Master (HM)
(N. Yozbatiran et al., 2011)	Case study	RiceWrist	Both sides	Joint movements: wrist flexion/extension, radial/ulnar deviation, forearm supination/pronation Target hitting exercises	(N. Yozbatiran et al., 2011)	Case study	RiceWrist
(Nuray Yozbatiran et al., 2012)	Case study	MAHI Exo-II	Both sides	Joint movements: elbow flexion/extension, forearm supination/pronation, wrist flexion/extension and radial/ulnar deviation Target hitting exercises	(Nuray Yozbatiran et al., 2012)	Case study	MAHI Exo-II

Outcomes

Almost all included studies investigated the following aspects: muscle strength, arm and hand function, and perceived fatigue or pain (Cortes et al., 2013; Francisco et al., 2017; Hwan Jung et al., 2019; Kim et al., 2019; Osuagwu et al., 2020; Pehlivan et al., 2014; Shimizu et al., 2017; N. Yozbatiran et al., 2011; Nuray Yozbatiran et al., 2012). In addition, Vanmulken et al. (2015) also assessed the usability, motivation and expectation and Osuagwu et al. (2020) the satisfaction perceived by the participants. Cortes et al. (2013) and Eng et al. (2011) investigated movement trajectory and movement speed. See Table 5**Fout! Verwijzingsbron niet gevonden.** for a detailed description of used outcome measures and study results.

Muscle strength

Muscle strength was measured by the Upper Extremity Muscle Strength (UEMS) or Manual Muscle Testing (MMT) (Cortes et al., 2013; Francisco et al., 2017; Hwan Jung et al., 2019; Kim et al., 2019; Pehlivan et al., 2014; Shimizu et al., 2017; N. Yozbatiran et al., 2011; Nuray Yozbatiran et al., 2012). These tests scored the key muscles chosen by the study. Typically, motor scores of elbow flexion/extension, wrist extension, finger flexion, and finger abduction were assessed (Cortes et al., 2013; Francisco et al., 2017; Hwan Jung et al., 2019; Kim et al., 2019; Pehlivan et al., 2014; Shimizu et al., 2017; N. Yozbatiran et al., 2011; Nuray Yozbatiran et al., 2012). Additionally, the grip of pinch force was assessed in a few studies using a hand-held dynamometer and pinch gauche (Francisco et al., 2017; Hwan Jung et al., 2019; Z. Lu et al., 2017; Osuagwu et al., 2020; Pehlivan et al., 2014; N. Yozbatiran et al., 2011).

Results differed between studies. According to Cortes et al. (2013) there were no significant changes in motor strength ($p = 0,4$). Kim et al. (2019) also reported no statistically significant changes in motor scores of key muscles. In contrast, Francisco et al. (2017) found significant increases in total UEMS scores after treatment, that maintained at six months follow-up ($p = 0,04$ and $p = 0,02$ respectively). The change in muscle strength was highest in elbow flexion

(6% increase) and little finger abduction (15%). Similarly, Hwan Jung et al. (2019) showed a significant increase in muscle strength, with no significant differences between the group with robotic training (RT) and occupational training (OT). Studies such as Shimizu et al. (2017), Yozbatiran et al. (2012) and Yozbatiran et al. (2011) reported both unchanged and increased motor scores, but these studies did not perform a statistical analysis. Therefore, interpretation of these results should be made with care. Yozbatiran et al. (2012) reported an increase in UEMS scores from seven to nine points and Yozbatiran et al. (2011) an increase from eight to nine.

Similar results were found in the assessment of the grip and pinch force. Francisco et al. (2017) found significant increases in both (p= 0,02 and p= 0,01 respectively), both after treatment and follow-up for the pinch force (p= 0,02). Osuagwu et al. (2020) reported significant increases in key grip strength, from initial assessment to week six, 12 and 18 (p= 0,0009893, p= 0,01629, p= 0,008444 respectively). Improvements in jaw grip strength were also reported, with a significant increase from initial assessment to week six, 12 and 18 (p= 0,001438, p= 0,01017, p= 0,008062 respectively). In contrast, Hwan Jung et al. (2019) reported significant improvements in the OT group for the tip pinch and three-jaw chuck (p= 0,044 and p= 0,03 respectively), yet no significant improvements in the RT group. Changes between these groups were not found statistically significant. Yozbatiran et al. (2011) reported no change in the grip force, but an increase in pinch strength of the right and left extremity (zero to two and six point five to ten respectively). No statistical analysis was conducted. Similarly, Pehlivan et al. (2014) and Lu et al. (2017) reported improvements but no statistical analysis was done.

Arm and hand function

Tests such as the Action Research Arm Test (ARAT), the Graded Redefined Assessment of Strength, Sensibility and Prehension (GRASSP) and the Jebsen-Taylor Hand function Test (JTHFT) were frequently used to assess the arm and hand function of the participants (Hwan Jung et al., 2019; Z. Lu et al., 2017; Pehlivan et al., 2014; N. Yozbatiran et al., 2011; Nuray Yozbatiran et al., 2012). Francisco et al. (2017) found significant improvements in the total score of the JTHFT (p=0,04). Not all improvements on the subtest of the JTHFT were

maintained after six months follow-up. In this study, three subjects exceeded the minimal clinically important difference (MCID) of five point 7 points in the ARAT score.

Pehlivan et al. (2014) reported improvements in JTHFT scores by a decrease of time needed to execute the tasks. Improvements in the ARAT were found but remained lower than the MCID of five point seven points. Similar results were found by Yozbatiran et al. (2012) where improvements on the ARAT were described, an increase from 41 to 49 points. Lu et al. (2017) reported gains on total scores of the GRASSP, with an increase of two points. Neither of the aforementioned studies performed statistical analysis.

In multiple studies, the Spinal Cord Independence Measure III (SCIM-III) was used to assess the level of independence of the participants (Francisco et al., 2017; Hwan Jung et al., 2019; Kim et al., 2019). Francisco et al. (2017) showed no significant differences after treatment. In Hwan Jung et al. (2019) both RT and OT groups improved significantly after treatment (p= 0,008 and p= 0,024 respectively). There was no statistically significant difference between the two groups. RT showed specific improvements in bathing and dressing upper extremity and grooming (p= 0,011, p= 0,028 and p= 0,025 respectively). Kim et al. (2019) reported no significant improvements in the SCIM-III scores with exception of the mobility (room and toilet) subscale. The median change in the RT group was one in comparison to zero in the OT group, with p-value of 0,02. Similarly, Yozbatiran et al. (2011) used the functional independence measure (FIM). They observed improved independence in activities such as grooming, dressing lower body, and going up/downstairs.

Less frequently used tests were the van Lieshout test (Vanmulken et al., 2015), the Box and Block Test (BBT) (Z. Lu et al., 2017), the Toronto Rehabilitation Institute Hand Function Test (TRI-HFT) (Osuagwu et al., 2020). Lu et al. (2017) reported an increased number of moved blocks in the BBT (seven blocks extra). There was no mention of statistical significance. Vanmulken et al. (2015) reports that they found no large improvements in the Van Lieshout test. Osuagwu et al. (2020) found almost no significant increase in scores on the subtests of the TRI-HFT.

Perceived pain and fatigue

Multiple studies used the Visual Analogue Scale (VAS) after each training session to assess pain and fatigue in their participants. Participants reported an increase in level of fatigue immediately after the session, but this increase did not result in missing a session (Cortes et al., 2013; Francisco et al., 2017; Pehlivan et al., 2014; N. Yozbatiran et al., 2011; Nuray Yozbatiran et al., 2012). It was not used to assess the progression of intensity of the training session.

Study	Measured outcomes	Results
(Cortes et al., 2013)	Kinematics: aim, deviation, mean speed, peak speed, movement smoothness, duration of movement. Clinical outcomes: UEMS, MAS and VAS Neurophysiological outcomes: resting motor threshold, MEP and MEP facilitation.	Kinematics: significant improvements in aim and smoothness (p= 0,03 and p= 0,03). No changes in deviation, mean speed, peak speed and duration of movements were found. Clinical outcomes: no significant changes in motor strength (p= 0,4). No changes in MAS (p= 0,43). No changes in pain level (p= 0,99). Neurophysiological outcomes: no changes
(Eng et al., 2011)	Average movement time (Ta) Trajectory variability envelope (Tjv)	Ta: improvements observed for the left side, values approached that of healthy control. Smaller improvements for the right side (flexion and ulnar deviation). Tjv: Very small changes (L > R), greatest for forearm supination
(Francisco et al., 2017)	UEMS and grip/pinch strength (handheld dynamometer). ARAT and JTHFT SCIM-II Level of perceived pain and fatigue.	UEMS: increase of 6% in elbow extension, 15% increase in 5th finger AB. Higher gains in the affected side (p=0,04). Gain in total UEMS was significant after treatment and maintained at 6m follow-up. Grip/pinch strength: significant improvements after treatment and maintained at 6m follow-up. Higher gains in the more affected side (p=0,04 and p=0,02). JTHFT and ARAT: significant improvements in function, maintained at 6m follow-up. In 3 subjects ARAT MCID of 5,7 was exceeded. Change in the less affected arm was higher (p=0,02). SCIM-II: no statistically significant difference after treatment or follow-up. Pain/fatigue: no significant increase. Fatigue increased after each session, but no session was missed.
(Hwan Jung et al., 2019)	GRASSP UEMS Grip & pinch strength SCIM-III	GRASSP: statistically significant increase in total scores in both groups. RT: shoulder AB, elbow flexion and extension, 2-5th MCP extension. Improvements in cylindrical grasp, lateral key pinch and total qualitative prehension, coins in slot. OT: shoulder AB, wrist extension, 5th MCP AB. Significant improvements in total score of quantitative prehension. No significant difference between groups. UEMS: both groups increased significantly. Grip strength: RT no significant improvements, OT significant improvements in tip pinch and three-jaw chuck items. No significant difference in UEMS and grip/pinch strength between groups. SCIM-III: RT showed significant improvements in bathing-upper, dressing-upper and grooming. OT showed improvements in dressing-lower. No significant increase in total score in either group. Significant difference between two groups on bathing-upper items.
(Kim et al., 2019)	UEMS SCIM-III	UEMS: Median change in UEMS in RT group was 1 (OT =0) (p=0,03). No statistically significant changes in MRC scale of key muscles. SCIM-III: Median change of SCIM-III score in RT group was 7 (OT=0) (p<0,01). Median change of mobility (subscale SCIM-III) in the RT group was 1 (OT=0) (p=0,02). Small improvements in motor strength and SCIM-III scores in the RT group, but no statistically significant differences between the groups.

(Pehlivan et al., 2014)	TRI-HFT Grip strength (pinch meter). MAS of AB/AD, extensors and flexors of shoulder, extensor/flexors of elbow, wrist, fingers and thumb. Quebec user evaluation of satisfaction with assistive technology (QUEST) for health state.	TRI-HFT: Object manipulation: significant increase from initial to week 6 (p = 0,013358), but not for week 12 and 18 (p= 0,1466 and p=0,051762. Wooden blocks component: no effect (p= 0,31988). Instrumented cylinder component: no significant difference between initial, week 6, week 12 and week 18 (p= 0,059285, p= 0,29287, p= 0,05098). Instrumented credit card: no significant difference between initial, week 6, week 12 and week 18 (p= 0,018102, p= 0,32797, p= 0,051542). Wooden bar component: significant increase in hand function from initial to week 6 and week 12, and almost significant change for week 18 (p= 0,0086347, p= 0,0076498, p= 0,017671). Grip strength: key grip strength: significant increase from initial to week 6, 12 and 18 (p= 0,0009893, p= 0,01629, p= 0,008444). Jaw grip strength: significant increase from initial to week 6, 12 and 18 (p= 0,001438, p= 0,01017, p= 0,008062). Tip to tip grip strength: no main effect (p= 0,4604). MAS: no significant difference. MAS of thumb showed significant difference between initial and week 6 (p= 0,0053), and almost significant change between initial and week 12 (p= 0,0212). This improvement was not sustained through week 18. SF-36: No significant change in total score.
(Osuagwu et al., 2020)	UEMS and grip/pinch force JTHFT and ARAT Level of fatigue and discomfort with VAS	JTHFT: improvements by decrease of time needed to execute tasks. ARAT: improvement in pinch and grip strength but remained lower than MCID of 5,7 points. Grip strength: improves from 11 to 14 kg VAS: varied after each session but no sessions were missed.
(Lu et al., 2017)	Grip force (JAMAR and handheld dynamometer) Box and Block test. GRASSP	Grip force: 13,5 kg to 19,6kg. Box and Block test: transported 7 extra blocks (39). GRASSP: gained 2 points on total score. Control accuracy improved from 71,3% to 95,8%.
(Shimizu et al., 2017)	EMG to assess muscle activation of the trapezius, biceps brachii, infraspinatus and triceps brachii. MMT Barthel index FIM	EMG: / Barthel index and FIM scores remained unchanged, MMT: increase in bilateral biceps
(Vanmulken et al., 2015)	Usability: USE Motivation and expectation: IMI Credibility/expectancy questionnaire Van Lieshout test SCIM-III Muscle strength (measured by microfet)	By therapists: USE-questionnaire 65,1%. By participants: IMI 66% Credibility/expectancy 60,7% No discernable differences at activity level Muscle strength: 2 participants had changes
(N. Yozbatiran et al., 2011)	UEMS and grip/pinch strength JTHFT FIM Pain and fatigue after each session.	UEMS: increased muscle strength observed on the right side only. Grip strength: changes were observed on the left side. Pinch strength: changes were observed on both sides. FIM: independence was observed in activities such as grooming, dressing lower body and going up/downstairs. Hand functions such as manipulating objects, grasping and lifting showed improvements. No significant increase in pain during sessions, fatigue slightly increased but no session was missed.

(Nuray Yozbatiran et al., 2012)	UEMS JTHF and ARAT Pain and fatigue after each session.	UEMS: score of wrist extensor (C6) and finger flexor (C8) increased from 1 to 2 on the right side, MMT of finger abductor (T1) increased from 2 to 3 on the left side. ARAT: functional improvements on ARAT only on the left side. No significant increase in pain/discomfort. Increase in fatigue after the session but no sessions were missed.

Abbreviations:
UEMS: Upper Extremity Motor Score
JTHFT: Jebsen-Taylor Hand Function Test
ARAT: Action Research Arm Test
GRASSP: Graded Redefined Assessment of Strength, Sensation and Prehension
SCIM-III: Spinal Cord Independence Measure
FIM: Functional Independence Measure
MAS: Modified Ashworth Scale
VAS: Visual Analogue Scale
TRI-HFT: Toronto Rehabilitation Institute hand function test
USE: Usefulness, satisfaction and ease-of-use questionnaire
IMI: intrinsic motivation inventory
MEP: Motor evoked potential

Table 5: Overview outcomes

5. Discussion

5.1 Quality of the study

The overall quality of the included studies was low, as expected. The use of robotics in SCI rehabilitation is still not fully researched, especially upper limb rehabilitation. This meant that only a scarce number of studies were available. There were, however, two RCTs included. These were of better quality, thus preliminary conclusions can be made of those two.

5.2 Reflection research question

Together, the findings of all included studies suggest that a robotic rehabilitation program improves muscle strength and functionality of the hand or arm, although not all studies could support their reported improvements with statistically significant values. In most studies, functional improvements did not result in higher independence of the participants. Only in the studies of Hwan Jung et al. (2019), Kim et al. (2019) and Kim et al. (2019) there were significant differences in the SCIM-III scores and Yozbatiran et al. (2011) reported improvements on the FIM scores.

The KNGF guidelines for stroke state that rehabilitation should be functional, preferably in a patient's home or a well-known environment, and exercises should be task specific. There was only one study that performed the intervention in the home of patients, this was the study of Osuagwu et al. (2020). The soft robotic glove (SEM Glove) was used, a relatively small application device compared to the robotic devices described in other articles. This lack of home-intervention in robotic rehabilitation can be explained by an obvious limitation: robotic devices are not yet made in a size that it is feasible for a patient to take it home with him. Vanmulken et al. (2015) let the patients choose which specific ADL-activities would be practiced with the help of the robotic device. This correlates with the KNGF guidelines that the exercises are chosen individually and should be task-specific. Multiple studies did however try to incorporate semi-task-specific exercises, such as target hitting. These were often performed in the form of a game, which served as a motivation for the patients (Eng et al., 2011; Osuagwu et al., 2020; Yozbatiran et al., 2011; Yozbatiran et al., 2012).

Although there is no clear guideline on training amount or intensity, research in stroke patients showed that a higher amount of practice hours results in improvements in muscle strength, movement coordination, improved functionality and maybe even improved independence (J M Veerbeek et al., 2014). A greater amount of training can produce lasting physiological changes in the motor neural network and therefore have an influence on functional outcomes (Lang et al., 2015). Similar, yet preliminary results are found in SCI rehabilitation (Buehner et al., 2012; Fehlings et al., 2017). In this review, when improvements were compared to the hours spent training with the robotic device, a trend, however small, is visible: most studies that reported no or only slight changes in functional outcomes or level of independence, were studies with 18 trained hours or less (Cortes et al., 2013; Shimizu et al., 2017; Vanmulken et al., 2015). In contrast, Lu et al. (2017), Yozbatiran et al. (2011), Yozbatiran et al. (2012) and Francisco et al. (2017) all spent 30 hours or more training with a robot and reported greater improvements. Hwan Jung et al. (2019) and Kim et al. (2019) reported significant improvements as well, although they only spent ten hours training with a robotic device. This could be explained by the additional functional task training exercises they implemented in their intervention, in this manner they reached a total of 40 and 17,5 training hours, respectively. Many included studies did not perform statistical analyses, so conclusions cannot be made easily. Still, this trend may suggest that a greater amount of training hours influences functional improvements.

Some studies suggest that a distributed training, sessions scheduled over longer intervals, will be more effective than massed training schedules in optimizing motor outcome (Hogan et al., 2006). This suggest that an intervention program spread across a longer time would be more beneficial for functional outcomes. No trend was visible throughout the results of the included studies.

Since training volume can not only be changed by training hours but also number of repetitions (Lang et al., 2015), suggestions have been made that a greater amount of repetitions show greater improvements (Zbogar et al., 2017). Data about the number of repetitions in included studies was limited, therefore no clear deduction could be made. In addition to repetitions, intensity of training can be increased by adding a greater load or by evolving to a more difficult movement (Zbogar et al., 2017). On this matter, included studies did not give information either, mostly mentioning that training intensity was progressed by

adding number of repetitions, less rest in between exercises and changing amount of resistance (Eng et al., 2011; Kim et al., 2019; Z. Lu et al., 2017; N. Yozbatiran et al., 2011; Nuray Yozbatiran et al., 2012).

Multiple studies, in both stroke and SCI rehabilitation, find significant improvements with the use of robotic training (Nam et al., 2017; J M Veerbeek et al., 2014; Zariffa et al., 2012). Yet to this day, it is unclear whether robotic training is more effective in rehabilitation than other interventions (J M Veerbeek et al., 2014). The two RCTs included in this systematic review used a robotic trained group and a control group with conventional therapy. They found significant changes in functional outcomes, yet no significant difference between the robotic trained group and the control group (Hwan Jung et al., 2019; Kim et al., 2019).

Given the low quality of the included studies, a conclusion on whether training volume, and all its aspects, within robotic rehabilitation has an influence on functional outcomes in patients with cervical SCI could not be made. Further research is necessary to give a clear insight in this matter.

5.3 Limitations and strengths

As mentioned before, the quality of the studies included in this review are poor and deductions must be made with care. Secondly, the number of participants of the included articles were low and thus the statistical power of these were not sufficient. Hence, no concrete conclusions could be drawn.

As for strengths, study selection and quality assessment were performed independently by both reviewers, discrepancies were discussed and finalized. Also, this review clearly shows a gap in scientific evidence around robotic rehabilitation for upper extremity in SCI patients, as well as emphasizes the need for clarity in necessary training volume and intensity during rehabilitation.

5.4 Recommendations for future research

Further studies are needed to see if robotic training is more efficient than other interventions, or whether it is an easy additional form of training to use during SCI rehabilitation. Since there is limited data available about the number of repetitions, training hours, training intensity... future studies should focus on checking the influence of training volume on functional outcomes. Furthermore, research is necessary to see whether specific volumes, repetitions or training frequencies can insure the greatest functional improvements.

6. Conclusion

Findings suggest that the use of robotics during SCI rehabilitation is feasible and can improve muscle strength and functionality in arm and hand function, and perhaps even improve the level of independence of SCI patients. Preliminary findings also suggest that a greater amount of training may result in greater functional improvements, though further research is necessary to clear this out. Further research is also necessary to see whether specific training volumes or intensities result in optimal improvements.

7. References

Anderson, K. D. (2004, October). Targeting recovery: Priorities of the spinal cord-injured population. *Journal of Neurotrauma*. J Neurotrauma. https://doi.org/10.1089/neu.2004.21.1371

Buehner, J. J., Forrest, G. F., Schmidt-Read, M., White, S., Tansey, K., & Basso, D. M. (2012). Relationship between ASIA examination and functional outcomes in the neurorecovery network locomotor training program. *Archives of Physical Medicine and Rehabilitation*, *93*(9), 1530–1540. https://doi.org/10.1016/j.apmr.2012.02.035

Cochrane Collaboration. (2021). Beoordelingsformulieren en andere downloads | Cochrane Netherlands. Retrieved April 27, 2021, from https://netherlands.cochrane.org/beoordelingsformulieren-en-andere-downloads

Cortes, M., Elder, J., Rykman, A., Murray, L., Avedissian, M., Stampa, A., … Edwards, D. J. (2013). Improved motor performance in chronic spinal cord injury following upper-limb robotic training. *NeuroRehabilitation*, *33*(1), 57–65. https://doi.org/10.3233/NRE-130928

Eng, D. P., Kadivar, Z., Sullivan, J. L., Pehlivan, A. U., O'Malley, M. K., Francisco, G. E., & Yozbatiran, N. (2011). Spatial and temporal movement characteristics after robotic training of arm and hand: A case study of a person with incomplete spinal cord injury (pp. 1711–1716). Institute of Electrical and Electronics Engineers (IEEE). https://doi.org/10.1109/iros.2011.6095134

Fehlings, M. G., Tetreault, L. A., Wilson, J. R., Kwon, B. K., Burns, A. S., Martin, A. R., … Harrop, J. S. (2017). A Clinical Practice Guideline for the Management of Acute Spinal Cord Injury: Introduction, Rationale, and Scope. https://doi.org/10.1177/2192568217703387

Fitle, K. D., Pehlivan, A. U., & O'Malley, M. K. (2015). A robotic exoskeleton for rehabilitation and assessment of the upper limb following incomplete spinal cord injury. In *Proceedings - IEEE International Conference on Robotics and Automation* (Vol. 2015-June, pp. 4960–4966). Institute of Electrical and Electronics Engineers Inc. https://doi.org/10.1109/ICRA.2015.7139888

Francisco, G. E., Yozbatiran, N., Berliner, J., O'Malley, M. K., Pehlivan, A. U., Kadivar, Z., … Boake, C. (2017). Robot-Assisted Training of Arm and Hand Movement Shows Functional Improvements for Incomplete Cervical Spinal Cord Injury. *American Journal of Physical Medicine & Rehabilitation*, *96*(10), S171–S177. https://doi.org/10.1097/PHM.0000000000000815

Hogan, N., Krebs, H. I., Rohrer, B., Palazzolo, J. J., Dipietro, L., Fasoli, S. E., … Volpe, B. T. (2006). Motions or muscles? Some behavioral factors underlying robotic assistance of motor recovery, *43*(5), 605–618. https://doi.org/10.1682/JRRD.2005.06.0103

Hwan Jung, J., Jin Lee, H., Youn Cho, D., Lim, J.-E., Suk Lee, B., Hyun Kwon, S., … Jeong Lee, S. (2019). Effects of Combined Upper Limb Robotic Therapy in Patients With Tetraplegic Spinal Cord Injury. *Annals of Rehabilitation Medicine Original Article Ann Rehabil Med*, *43*(4), 445–457. https://doi.org/10.5535/arm.2019.43.4.445

Kang, Y., Ding, H., Zhou, H., Wei, Z., Liu, L., Pan, D., & Feng, S. (2017). Epidemiology of worldwide spinal cord injury: a literature review. *Journal of Neurorestoratology*, *Volume 6*, 1–9. https://doi.org/10.2147/jn.s143236

Kim, J., Lee, B. S., Lee, H. J., Kim, H. R., Cho, D. Y., Lim, J. E., … Han, Z. A. (2019). Clinical efficacy of upper limb robotic therapy in people with tetraplegia: a pilot randomized controlled trial. *Spinal Cord*, *57*(1), 49–57. https://doi.org/10.1038/s41393-018-0190-z

Kirshblum, S. C., Burns, S. P., Biering-Sorensen, F., Donovan, W., Graves, D. E., Jha, A., … Waring, W. (2011). International standards for neurological classification of spinal cord injury (Revised 2011). *Journal of Spinal Cord Medicine*. Taylor & Francis. https://doi.org/10.1179/204577211X13207446293695

Krebs, H. I., Dipietro, L., Levy-Tzedek, S., Fasoli, S. E., Rykman-Berland, A., Zipse, J., … Hogan, N. (2008, July). A paradigm shift for rehabilitation robotics. *IEEE Engineering in Medicine and Biology Magazine*. NIH Public Access. https://doi.org/10.1109/MEMB.2008.919498

Lang, C. E., Lohse, K. R., & Birkenmeier, R. L. (2015). Dose and timing in neurorehabilitation: Prescribing motor therapy after stroke. https://doi.org/10.1097/WCO.0000000000000256

Lu, X., Battistuzzo, C. R., Zoghi, M., & Galea, M. P. (2015, January 17). Effects of training on upper limb function after cervical spinal cord injury: A systematic review. *Clinical Rehabilitation*. SAGE Publications Ltd. https://doi.org/10.1177/0269215514536411

Lu, Z., Tong, K. Y., Shin, H., Stampas, A., & Zhou, P. (2017). Robotic Hand-Assisted Training for Spinal Cord Injury Driven by Myoelectric Pattern Recognition: A Case Report. *American Journal of Physical Medicine & Rehabilitation*, *96*(10), S146–S149. https://doi.org/10.1097/PHM.0000000000000798

Nam, K. Y., Kim, H. J., Kwon, S., Park, J.-W., Lee, H. J., & Yoo, A. (2017). Robot-assisted gait training (Lokomat) improves walking function and activity in people with spinal cord injury: a systematic review. https://doi.org/10.1186/s12984-017-0232-3

Osuagwu, B. A. C., Timms, S., Peachment, R., Dowie, S., Thrussell, H., Cross, S., … Taylor, J. (2020). Home-based rehabilitation using a soft robotic hand glove device leads to improvement in hand function in people with chronic spinal cord injury:a pilot study. *Journal of NeuroEngineering and Rehabilitation*, *17*(1). https://doi.org/10.1186/s12984-020-00660-y

Pehlivan, A. U., Sergi, F., Erwin, A., Yozbatiran, N., Francisco, G. E., & O'Malley, M. K. (2014). Design and validation of the RiceWrist-S exoskeleton for robotic rehabilitation after incomplete spinal cord injury. *Robotica*, *32*(8), 1415–1431. https://doi.org/10.1017/S0263574714001490

Shimizu, Y., Kadone, H., Kubota, S., Ikumi, A., Abe, T., Marushima, A., … Yamazaki, M. (2017, July 4). Active elbow flexion is possible in C4 quadriplegia using hybrid assistive limb (HAL®) technology: A case study. *Journal of Spinal Cord Medicine*. Taylor and Francis Ltd. https://doi.org/10.1080/10790268.2017.1305036

Singh, H., Unger, J., Zariffa, J., Pakosh, M., Jaglal, S., Craven, B. C., & Musselman, K. E. (2018, October 3). Robot-assisted upper extremity rehabilitation for cervical spinal cord injuries: a systematic scoping review. *Disability and Rehabilitation: Assistive Technology*. Taylor and Francis Ltd. https://doi.org/10.1080/17483107.2018.1425747

Vanmulken, D. A. M. M., Spooren, A. I. F., Bongers, H. M. H., & Seelen, H. A. M. (2015). Robot-assisted task-oriented upper extremity skill training in cervical spinal cord injury: A feasibility study. *Spinal Cord*, *53*(7), 547–551. https://doi.org/10.1038/sc.2014.250

Veerbeek, J M, Van Wegen, E. E. H., Van Peppen, R. P. S., Hendriks, H. J. M., Rietberg, M. B., Van Der Wees, P. J., … Kwakkel, G. (2014). *KNGF-richtlijn Beroerte Praktijkrichtlijn*. Retrieved from www.fysionet-evidencebased.nl.

Veerbeek, Janne M., Langbroek-Amersfoort, A. C., Van Wegen, E. E. H., Meskers, C. G. M., & Kwakkel, G. (2017, February 1). Effects of Robot-Assisted Therapy for the Upper Limb after Stroke. *Neurorehabilitation and Neural Repair*. SAGE Publications Inc. https://doi.org/10.1177/1545968316666957

Yozbatiran, N., Berliner, J., Boake, C., O'Malley, M. K., Kadivar, Z., & Francisco, G. E. (2011). Robotic training and clinical assessment of forearm and wrist movements after incomplete spinal cord injury: A case study. In *IEEE International Conference on Rehabilitation Robotics* (Vol. 2011). IEEE Int Conf Rehabil Robot. https://doi.org/10.1109/ICORR.2011.5975425

Yozbatiran, Nuray, Berliner, J., O'Malley, M. K., Pehlivan, A. U., Kadivar, Z., Boake, C., & Francisco, G. E. (2012). Robotic training and clinical assessment of upper extremity movements after spinal cord injury: A single case report. *Journal of Rehabilitation Medicine*, *44*(2), 186–188. https://doi.org/10.2340/16501977-0924

Yozbatiran, Nuray, & Francisco, G. E. (2019, May 1). Robot-assisted Therapy for the Upper Limb after Cervical Spinal Cord Injury. *Physical Medicine and Rehabilitation Clinics of North America*. W.B. Saunders. https://doi.org/10.1016/j.pmr.2018.12.008

Zariffa, J., Kapadia, N., Kramer, J., Taylor, P., Alizadeh-Meghrazi, M., Zivanovic, V., … Steeves, J. D. (2012). Feasibility and efficacy of upper limb robotic rehabilitation in a subacute cervical spinal cord injury population. *Spinal Cord*, *50*, 220–226. https://doi.org/10.1038/sc.2011.104

Zbogar, D., Eng, J. J., Miller, W. C., Krassioukov, A. V, & Verrier, M. C. (2017). Movement repetitions in physical and occupational therapy during spinal cord injury rehabilitation. *Nature Publishing Group*, *55*, 172–179. https://doi.org/10.1038/sc.2016.129

8. Appendix

CONTRACT WETENSCHAPPELIJKE STAGE DEEL 1

Datum: 7/11/2020

Student(e)1: Hanne Rombaut

Student(e) 2: Eline Bollen

Promotor: Annemie Spooren

Copromotor: /

Situering masterproef:

☐ Vormt onderdeel van lopend onderzoeksproject, nl. ……

☒ Vormt onderdeel van opstartend onderzoeksproject, nl. ……..

☐ Individuele studie

☐ Andere, nl. ……..…

Nederlandstalige werktitel masterproef:

/

Engelstalige werktitel masterproef (indien van toepassing)

Upper extremity training and rehabilitation technology in C-SCI

Voorlopige onderzoeksvraag literatuurstudie (indien gekend)

/

Formatkeuze van format MP1

☒ Centrale format (conform met masterproefrichtlijnen)

☐ Alternatieve format (zie richtlijnen alternatieve format), nl.

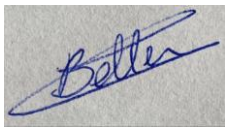
Uitsluitend van toepassing indien CENTRAL FORMATKEUZE

Doelstelling	Akkoord	Niet akkoord	NVT
1. De student(e) formuleert (in samenspraak met de promotor) een duidelijke vraag in functie van de literatuurstudie. Duid NVT aan indien de vraagstelling voor de literatuurstudie volledig door de promotor wordt aangereikt en formuleer een doelstelling voor de student(e): ……	☑	☐	☐
2. De student(e) voert een literatuurstudie uit conform de richtlijnen MP deel 1.	☑	☐	
3. De student(e) schrijft de literatuurstudie uit in academische taal conform met de richtlijnen MP deel 1.	☑	☐	
4. De student(e) formuleert, op grond van de gerealiseerde literatuurstudie een onderzoeksvraag voor het eigenlijke wetenschappelijke onderzoek (MP 2). Duid NVT aan indien de student(e) deelneemt aan een lopend onderzoeksproject en de onderzoeksvraag al geformuleerd is en formuleer een doelstelling voor de student(e): ……..	☑	☐	☐
5. De student(e) kiest een onderzoeksdesign en maakt een kritische keuze van de te hanteren methodologie en materialen. Duid NVT aan indien de student(e) gebruik maakt van een uitgewerkt onderzoeksdesign (lopend onderzoeksproject) en formuleer een doelstelling voor de student(e) ……..	☑	☐	☐
6. De student(e) schrijft de methodologiesectie van zijn/haar onderzoek uit conform de richtlijnen MP deel 1. Duid NVT aan indien de student(e) gebruik maakt van een uitgewerkt onderzoeksprotocol (lopend onderzoeksproject) en formuleer een doelstelling voor de student(e) ……	☑	☐	☐
7. De student(e) schrijft het onderzoeksprotocol uit in academische taal conform met de richtlijnen MP1.	☑	☐	
8. De student(e) voert reeds in deze fase (een deel van) de data acquisitie uit. Duid NVT aan indien de data-acquisitie voltooid wordt/werd zonder inbreng van de student(e) en formuleer een doelstelling voor de student(e)……	☑	☐	☐
9. De student(e) voert reeds in deze fase (een deel van) de data verwerking uit. Duid NVT aan indien de dataverwerking voltooid wordt/werd zonder inbreng van de student(e) en formuleer een doelstelling voor de student(e)……	☑	☐	☐
10. Bijkomende afspraken: ✓ ✓	☐	☐	☐

Datum & handtekening student(e)

7-11-2020

Eline bollen



Datum & handtekening promotor

Hanne Rombaut

Verklaring op Eer

Ondergetekende, student aan de Universiteit Hasselt (UHasselt), faculteit Revalidatiewetenschappen aanvaardt de volgende voorwaarden en bepalingen van deze verklaring:

1. Ik ben ingeschreven als student aan de UHasselt in de opleiding Revalidatiewetenschappen en kinesitherapie, waarbij ik de kans krijg om in het kader van mijn opleiding mee te werken aan onderzoek van de faculteit Revalidatiewetenschappen aan de UHasselt. Dit onderzoek wordt beleid door Annemie Spooren en kadert binnen het opleidingsonderdeel Masterproef deel 1. Ik zal in het kader van dit onderzoek creaties, schetsen, ontwerpen, prototypes en/of onderzoeksresultaten tot stand brengen in het domein van Neurorevalidatie (hierna: "De Onderzoeksresultaten").

2. Bij de creatie van De Onderzoeksresultaten doe ik beroep op de achtergrondkennis, vertrouwelijke informatie[1], universitaire middelen en faciliteiten van UHasselt (hierna: de "Expertise").

3. Ik zal de Expertise, met inbegrip van vertrouwelijke informatie, uitsluitend aanwenden voor het uitvoeren van hogergenoemd onderzoek binnen UHasselt. Ik zal hierbij steeds de toepasselijke regelgeving, in het bijzonder de Algemene Verordening Gegevensbescherming (EU 2016-679), in acht nemen.

4. Ik zal de Expertise (i) voor geen enkele andere doelstelling gebruiken, en (ii) niet zonder voorafgaande schriftelijke toestemming van UHasselt op directe of indirecte wijze publiek maken.

5. Aangezien ik in het kader van mijn onderzoek beroep doe op de Expertise van de UHasselt, draag ik hierbij alle bestaande en toekomstige intellectuele eigendomsrechten op De Onderzoeksresultaten over aan de UHasselt. Deze overdracht omvat alle vormen van intellectuele eigendomsrechten, zoals onder meer – zonder daartoe beperkt te zijn – het auteursrecht, octrooirecht, merkenrecht, modellenrecht en knowhow. De overdracht geschiedt in de meest volledige omvang, voor de gehele wereld en voor de gehele beschermingsduur van de betrokken rechten.

6. In zoverre De Onderzoeksresultaten auteursrechtelijk beschermd zijn, omvat bovenstaande overdracht onder meer de volgende exploitatiewijzen, en dit steeds voor de hele beschermingsduur, voor de gehele wereld en zonder vergoeding:

   - het recht om De Onderzoeksresultaten vast te (laten) leggen door alle technieken en op alle dragers;
   - het recht om De Onderzoeksresultaten geheel of gedeeltelijk te (laten) reproduceren, openbaar te (laten) maken, uit te (laten) geven, te (laten) exploiteren en te (laten) verspreiden in eender welke vorm, in een onbeperkt aantal exemplaren;
   - het recht om De Onderzoeksresultaten te (laten) verspreiden en mee te (laten) delen aan het publiek door alle technieken met inbegrip van de kabel, de satelliet, het internet en alle vormen van computernetwerken;
   - het recht De Onderzoeksresultaten geheel of gedeeltelijk te (laten) bewerken of te (laten) vertalen en het (laten) reproduceren van die bewerkingen of vertalingen;

[1] Vertrouwelijke informatie betekent alle informatie en data door de UHasselt meegedeeld aan de student voor de uitvoering van deze overeenkomst, inclusief alle persoonsgegevens in de zin van de Algemene Verordening Gegevensbescherming (EU 2016/679), met uitzondering van de informatie die (a) reeds algemeen bekend is; (b) reeds in het bezit was van de student voor de mededeling ervan door de UHasselt; (c) de student verkregen heeft van een derde zonder enige geheimhoudingsplicht; (d) de student onafhankelijk heeft ontwikkeld zonder gebruik te maken van de vertrouwelijke informatie van de UHasselt; (e) wettelijk of als gevolg van een rechterlijke beslissing moet worden bekendgemaakt, op voorwaarde dat de student de UHasselt hiervan schriftelijk en zo snel mogelijk op de hoogte brengt.

- het recht De Onderzoeksresultaten te (laten) bewerken of (laten) wijzigen, onder meer door het reproduceren van bepaalde elementen door alle technieken en/of door het wijzigen van bepaalde parameters (zoals de kleuren en de afmetingen).

De overdracht van rechten voor deze exploitatiewijzen heeft ook betrekking op toekomstige onderzoeksresultaten tot stand gekomen tijdens het onderzoek aan UHasselt, eveneens voor de hele beschermingsduur, voor de gehele wereld en zonder vergoeding.

Ik behoud daarbij steeds het recht op naamvermelding als (mede)auteur van de betreffende Onderzoeksresultaten.

7. Ik zal alle onderzoeksdata, ideeën en uitvoeringen neerschrijven in een "laboratory notebook" en deze gegevens niet vrijgeven, tenzij met uitdrukkelijke toestemming van mijn UHasseltbegeleider Annemie Spooren.

8. Na de eindevaluatie van mijn onderzoek aan de UHasselt zal ik alle verkregen vertrouwelijke informatie, materialen, en kopieën daarvan, die nog in mijn bezit zouden zijn, aan UHasselt terugbezorgen.

Gelezen voor akkoord en goedgekeurd,

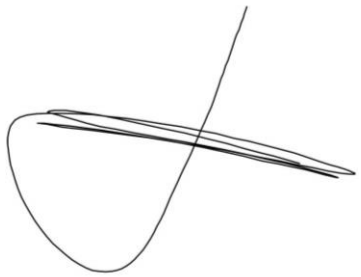
Naam: Hanne Rombaut

Adres: Haterbeekstraat 90, 3200 Aarschot

Geboortedatum en –plaats : 10/03/1996 te Leuven

Datum:8/11/2020

Handtekening:



Verklaring op Eer

Ondergetekende, student aan de Universiteit Hasselt (UHasselt), faculteit Revalidatiewetenschappen aanvaardt de volgende voorwaarden en bepalingen van deze verklaring:

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11. Ik zal de Expertise, met inbegrip van vertrouwelijke informatie, uitsluitend aanwenden voor het uitvoeren van hogergenoemd onderzoek binnen UHasselt. Ik zal hierbij steeds de toepasselijke regelgeving, in het bijzonder de Algemene Verordening Gegevensbescherming (EU 2016-679), in acht nemen.

12. Ik zal de Expertise (i) voor geen enkele andere doelstelling gebruiken, en (ii) niet zonder voorafgaande schriftelijke toestemming van UHasselt op directe of indirecte wijze publiek maken.

13. Aangezien ik in het kader van mijn onderzoek beroep doe op de Expertise van de UHasselt, draag ik hierbij alle bestaande en toekomstige intellectuele eigendomsrechten op De Onderzoeksresultaten over aan de UHasselt. Deze overdracht omvat alle vormen van intellectuele eigendomsrechten, zoals onder meer – zonder daartoe beperkt te zijn – het auteursrecht, octrooirecht, merkenrecht, modellenrecht en knowhow. De overdracht geschiedt in de meest volledige omvang, voor de gehele wereld en voor de gehele beschermingsduur van de betrokken rechten.

14. In zoverre De Onderzoeksresultaten auteursrechtelijk beschermd zijn, omvat bovenstaande overdracht onder meer de volgende exploitatiewijzen, en dit steeds voor de hele beschermingsduur, voor de gehele wereld en zonder vergoeding:

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[2] Vertrouwelijke informatie betekent alle informatie en data door de UHasselt meegedeeld aan de student voor de uitvoering van deze overeenkomst, inclusief alle persoonsgegevens in de zin van de Algemene Verordening Gegevensbescherming (EU 2016/679), met uitzondering van de informatie die (a) reeds algemeen bekend is; (b) reeds in het bezit was van de student voor de mededeling ervan door de UHasselt; (c) de student verkregen heeft van een derde zonder enige geheimhoudingsplicht; (d) de student onafhankelijk heeft ontwikkeld zonder gebruik te maken van de vertrouwelijke informatie van de UHasselt; (e) wettelijk of als gevolg van een rechterlijke beslissing moet worden bekendgemaakt, op voorwaarde dat de student de UHasselt hiervan schriftelijk en zo snel mogelijk op de hoogte brengt.

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- het recht De Onderzoeksresultaten te (laten) bewerken of (laten) wijzigen, onder meer door het reproduceren van bepaalde elementen door alle technieken en/of door het wijzigen van bepaalde parameters (zoals de kleuren en de afmetingen).

De overdracht van rechten voor deze exploitatiewijzen heeft ook betrekking op toekomstige onderzoeksresultaten tot stand gekomen tijdens het onderzoek aan UHasselt, eveneens voor de hele beschermingsduur, voor de gehele wereld en zonder vergoeding.

Ik behoud daarbij steeds het recht op naamvermelding als (mede)auteur van de betreffende Onderzoeksresultaten.

15. Ik zal alle onderzoeksdata, ideeën en uitvoeringen neerschrijven in een "laboratory notebook" en deze gegevens niet vrijgeven, tenzij met uitdrukkelijke toestemming van mijn UHasseltbegeleider Annemie Spooren.

16. Na de eindevaluatie van mijn onderzoek aan de UHasselt zal ik alle verkregen vertrouwelijke informatie, materialen, en kopieën daarvan, die nog in mijn bezit zouden zijn, aan UHasselt terugbezorgen.

Gelezen voor akkoord en goedgekeurd,

Naam: Eline Bollen_____

Adres: Biezenveld 53, 3590 Diepenbeek_____

Geboortedatum en –plaats :13/04/1999 te Hasselt_____

Datum:_09/11/2020_____

Handtekening: 

www.uhasselt.be
Campus Hasselt | Martelarenlaan 42 | BE-3500 Hasselt
Campus Diepenbeek | Agoralaan gebouw D | BE-3590 Diepenbeek
T + 32(0)11 26 81 11 | E-mail: info@uhasselt.be

UHASSELT
KNOWLEDGE IN ACTION

VOORTGANGSFORMULIER WETENSCHAPPELIJKE STAGE DEEL 1

DATUM	INHOUD OVERLEG	HANDTEKENINGEN
29/10/2020	Overleg topic	Promotor: Copromotor/begeleider: Student(e): Student(e):
04/01/2021	Overleg topic	Promotor: Copromotor/begeleider: Student(e): Student(e):
11/01/2021	Overleg onderzoeksvraag, zoekstrategie en planning	Promotor: Copromotor/begeleider: Student(e): Student(e):
09/02/2021	Overleg zoekstrategie	Promotor: Copromotor/begeleider: Student(e): Student(e):
18/02/2021	Overleg screening artikels	Promotor: Copromotor/begeleider: Student(e): Student(e):
26/02/2021	Overleg inclusie artikels en aantal artikels	Promotor: Copromotor/begeleider: Student(e): Student(e):
10/03/2021	Overleg checklist kwaliteitsbeoordeling en feedback bespreken	Promotor: Copromotor/begeleider: Student(e): Student(e):
01/04/2021	Overleg inleiding en feedback bespreken	Promotor: Copromotor/begeleider: Student(e): Student(e):
19/05/2021	Overleg feedback bespreken	Promotor: Copromotor/begeleider: Student(e): Student(e):
31/05/2021	Overleg feedback bespreken	Promotor: Copromotor/begeleider: Student(e): Student(e):

03/06/2021	Overleg feedback bespreken	Promotor: Copromotor/begeleider: Student(e): Student(e):
07/06/2021	Overleg feedback bespreken	Promotor: Copromotor/begeleider: Student(e): Student(e):
07/06/2021	Gunstig advies via e-mail	Promotor: Copromotor/begeleider: Student(e): Student(e):
	Niet-bindend advies: De promotor verleent hierbij het advies om de masterproef WEL/~~NIET~~ te verdedigen.	Promotor: Copromotor/begeleider: Student(e): Student(e):


toelating indiening MP deel 1 Inbox ×

Annemie SPOOREN 17:09 (2 minuten geleden)
aan Eline, mij

Dag Eline en hanne,
Hierbij geef ik jullie toestemming op MP deel 1 in te dienen, mits de aanpassingen die we vandaag besproken hebben/
mvg,
Annemie

--
Prof. Dr. Annemie Spooren
Tenure Track Professor
REVAL
Faculteit Revalidatiewetenschappen
UHasselt

0489/109007

LITERATUURSTUDIE	Gestelde deadline	Behaald op	Reflectie
De belangrijkste concepten en conceptuele kaders van het onderzoekdomein uitdiepen en verwerken	12/2020	12/2020	Ging volgens verwachting
De belangrijkste informatie opzoeken als inleiding op de onderzoeksvraag van de literatuurstudie	12/2020	12/2020	Ging volgens verwachting
De opzoekbare onderzoeksvraag identificeren en helder formuleren in functie van de literatuurstudie	12/2020	12/2020	Meerdere pogingen nodig gehad
De zoekstrategie op systematische wijze uitvoeren in relevante databanken	02/2021	02/2021	Ging volgens verwachting
De kwaliteitsbeoordeling van de artikels diepgaand uitvoeren	03/2021	03/2021	Ging volgens verwachting
De data-extractie grondig uitvoeren	03/2021	04/2021	Ging volgens verwachting
De bevindingen ïntegreren tot een synthese	05/2021	06/2021	Moeilijk om te schrijven met een voldoende duidelijke rode draad

ONDERZOEKSPROTOCOL	Gestelde deadline	Behaald op	Reflectie
De onderzoeksvraag in functie van het onderzoeksprotocol identificeren	04/2021	05/2021	Ging volgens verwachting
Het onderzoeksdesign bepalen en/of kritisch reflecteren over bestaande onderzoeksdesign	04/2021	05/2021	Ging volgens verwachting
De methodesectie (participanten, interventie, uitkomstmaten, data-analyse) uitwerken	04/2021	06/2021	Enkele bedenkingen rond bepaalde secties die zorgden voor vertraging

ACADEMISCHE SCHRIJVEN	Gestelde deadline	Behaald op	Reflectie
Het abstract tot he point schrijven	05/2021	06/2021	Ging volgens verwachting
De inleiding van de literatuurstudie logisch opbouwen	05/2021	06/2021	Moeizaam
De methodesectie van de literatuurstudie transparant weergegeven	04/2021	04/2021	Ging volgens verwachting
De resultatensectie afstemmen op de onderzoeksvragen	05/2021	06/2021	Moeizaam om terugkoppeling te maken naar onderzoeksvraag

In de discussiesectie de bekomen resultaten in een wetenschappelijke tekst integreren en synthetiseren	05/2021	06/2021	Volgens verwachting na overleg van discussiepunten
Het onderzoeksprotocol deskundig technisch uitschrijven	05/2021	06/2021	Ging volgens verwachting
Referenties correct en volledig weergeven	05/2021	06/2021	Ging volgens verwachting

ZELFSTUREND EN WETENSCHAPPELIJK DENLEN EN HANDELEN	**Aanvangsfase**	**Tussentijdse fase**	**Eindfase**
Een realistische planning opmaken, deadlines stellen en opvolgen	Moeizaam	Oke	Oke
Initiatief en verantwoordelijkheid opnemen ten aanzien van de realisatie van de wetenschappelijke stage	Oke	Oke	Oke
Kritisch wetenschappelijk denken	Moeizaam	Moeizaam	Oke
De contacten met de promotor voorbereiden en efficiënt benutten	Moeizaam	Oke	Oke
De richtlijnen van de wetenschappelijke stage autonoom opvolgen en toepassen	/	/	Oke
De communicatie met de medestudent helder en transparant voeren	Oke	Oke	Oke
De communicatie met de promotor/copromotor helder en transparant voeren	Oke	Oke	Oke
Andere verdiensten:	/	/	/

Part 2 Research protocol

1. Introduction

An estimated 291,000 people are living with spinal cord injury (SCI) in the United States alone, with approximately 17,700 new SCI's every year (Sheperd Center, 2021). Damage to the spinal cord can occur in a variety of ways, though the worldwide leading cause is external trauma such as vehicle accidents and falls (Kang et al., 2017). Non-traumatic injuries, e.g. tumors, spinal stenosis, and blood loss, are possible as well, though nearly not as prevalent (Sheperd Center, 2021). SCI leads to para-, quadri- or tetraplegia, depending on the level of injury, with varying degrees of loss in arm and hand function. According to Anderson (2004), people with SCI desire enough hand mobility and function so they can perform simple ADL-activities such as feeding, brushing their hair, using the telephone or computer etc.. Furthermore, all SCI participants from the study regarded exercise as a priority to their functional recovery and are eager and willing to work toward their improving function (Anderson, 2004; Fehlings et al., 2017).

Rehabilitation

Research in stroke patients showed that a higher number of hours practiced, both in acute and chronic stages, resulted in improvements in muscle strength, movement coordination, improved functionality and maybe even improved independence (Veerbeek et al., 2014). More hours spent training results in greater improvements in dissociative movements, walking distance and speed, ability to perform ADL-activities and quality of life (Veerbeek et al., 2014). In summary, a greater amount of training can produce lasting physiological changes in the motor neural network and therefore have an influence on functional outcomes. This brings forward an interesting matter: the influence of training volume and/or training intensity. Lang, Lohse, & Birkenmeier (2015) identifies training volume with following parameters: training frequency, duration, amount, and intensity. According to them, training amount can be altered by changing the number of repetition and actual therapy time. In addition to repetitions, intensity of training can be increased by adding a greater load or by evolving to a more difficult movement (Zbogar, Eng, Miller, Krassioukov, & Verrier, 2017). Animal studies showed improved locomotor capacity in SCI rehabilitation using several hundred to over a thousand repetitions. In humans, the motor-learning literature supports mid-hundreds to a thousand repetitions as well to improve upper- or

lower extremity functions (Zbogar et al., 2017). In reality, repetitions are noticeably lower in rehabilitation studies than those necessary for optimal neural plasticity with only a mean amount of 115 to 218 repetitions per session. Still, patients experienced improvements in clinical outcomes, yet Zbogar et al. (2017) says 'improvement is not the same as optimization, and the finding that therapy repetitions are vastly fewer than task-specific training protocols suggests that methods to increase repetitions would move us toward optimizing clinical outcomes.' However, Lang et al. (2015) states that the conclusion 'more is better' is too simple and suggests that the timing of training can interact with outcomes as well. 'More therapy may not be better in the first few hours and days after stroke and could lead to slower recovery.'

According to Fehlings et al. (2017) body weight–supported treadmill training as a recommended option for ambulation training in addition to conventional overground walking in acute rehabilitation. Similarly, Buehner et al. (2012) assessed the effect of locomotive training in chronic, incomplete SCI patients. They reported significant improvements in lower and upper extremity motor scores, six-minute walking test and ten-meter walking test. Clinically, this meant that 33% of non-ambulatory participants became ambulatory, 47% of slow walkers became faster walkers and 28% of participants went from C to D in AISA classification.

An explanation for these improvements can, in part, be found in the principle of motor learning and neuroplasticity. Repeated movement of motor tasks in a meaningful environment with a lot of feedback, both verbally and non-verbally, can have a positive effect on performing a specific task or ability. Several studies reported improvements in ability to perform a specific task after training in animal models. However, the effects of motor learning are only limited to the trained movement or task. They did not result in improvements on other aspects of motor function (de Leon, Hodgson, Roy, & Edgerton, 1994; Girgis et al., 2007). These findings suggest that task specificity is an important element to consider during rehabilitation. Some studies suggest that a distributed training, sessions scheduled over longer intervals, will be more effective than massed training schedules in optimizing motor outcomes (Hogan et al., 2006).

Use of technology during rehabilitation

During the rehabilitation of SCI patients, a robotic device makes an excellent tool to use during rehabilitation and lighten the workload of the therapist. All devices produce controlled movement or movement sequences with the ability to perform a high number of repetitions (Volpe et al., 2009). Many studies concluded that robotic training is a feasible and effective way to reach a high number of repetitions and therefore can hold a big advantage in a rehabilitative setting (Cortes et al., 2013; Eng et al., 2011; Lu, Tong, Shin, Stampas, & Zhou, 2017; Vanmulken, Spooren, Bongers, & Seelen, 2015; Veerbeek et al., 2014). Different kinds of robotic devices are available on the market. Some devices focus more on proximal movements, such as the ArmeoPower (Hwan Jung et al., 2019). Others, like the Amadeo, RiceWrist, Hand of hope etc.., focus on distal movements (Cortes et al., 2013; Francisco et al., 2017; Kim et al., 2019; Lu et al., 2017). Robotic devices can be categorized as end-effectors or exoskeletons.

In stroke rehabilitation, much research is available using robotic devices during rehabilitation, especially for lower limb function. For upper limb rehabilitation, research has shown that training of the hemiplegic shoulder and elbow using a robotic device leads to improvements of dissociative movements and muscle force of the arm. This for patients in both acute and chronic phases. To this day, it is yet unclear whether robotic training is more effective for improving arm-hand functionality compared to other interventions (Veerbeek et al., 2014).

Similar, yet fewer in numbers, research was done to investigate the effectiveness of robotic training and high doses of training in patients with SCI. In a review of SCI rehabilitation using a Lokomat, results showed that the use of a Lokomat with acute SCI patients lead to greater improvements in gait distance, strength, and functional level of mobility and independence compared to a control group without the use of a Lokomat. In chronic patients, improvements in speed and balance were observed. Overall, training with a Lokomat showed a promise in restoring functional walking (Nam et al., 2017). Even less research is available about robotic SCI rehabilitation for the upper extremity and results are contradictory. Zariffa et al. (2012) found no significant effect on muscle strength and functional performance in sub-acute patients with partial hand function after robotic

training combined with conventional therapy. Contrary, a case report by (Sledziewski, Schaaf, & Mount, 2012) reports improvements in active ROM, increased independence in self-care tasks, increased perceived capabilities of the upper extremity and improved strength. Our own systematic review found similar contradictory results where some studies reported improvements in functional outcomes and others reported none or not significant.

Since there is only preliminary research available about the use of robotics in SCI rehabilitation, this study will zoom in on this matter. Focus will be on the chronic, incomplete SCI population, to neutralize the effect of spontaneous recovery and neuroplasticity. Furthermore, since little data is available about optimal training volume, this study will try to bring this matter into focus by looking at the possible effects of a higher training volume on functional outcomes in this specific SCI population.

2. Aim of the study

2.1 Research question

This study will address the research question: What is the effect of high training volume with robotic rehabilitation on patients with chronic, incomplete cervical SCI on the arm and hand function?

2.2 Hypotheses

We hypothesize that with increasing training volume the improvements are greater than with a lower training volume.

3. Methods

3.1 Research design

This study is a randomized controlled trial in a single rehabilitation hospital. The participants will be randomized into two groups. This randomization will be generated via a computer program and blinded statistician. The participants will be allocated equally into the two groups. The intervention will take place over 12 weeks. Baseline assessment will be performed by a blinded assessor. Finally, there will be two independent, blinded physical therapists for the two intervention groups.

3.2 Participants

3.2.1 Inclusion criteria

We will include all participants who have a chronic incomplete cervical SCI (ASIA C-D). All participants must be 18 years or older. They cannot participate in other intervention studies focusing on arm/hand rehabilitation for the duration of this study or have participated in other studies 6 months prior to the start of this intervention. Additional therapy is allowed outside the intervention but cannot be any form of functional arm and/or hand therapy and should be limited to three times a week for one hour. Understanding instructions in Dutch is also necessary for participation.

3.2.2 Exclusion criteria

Patients with any other (neurological) health condition that could interfere with results will be excluded. A SCI on any other spinal level than cervical cannot be included in this study, as well as a complete SCI. Any form of cognitive impairments in the participants will also lead to exclusion.

3.2.3 Patients recruitment

The patients will be recruited from a single center for rehabilitation.

3.3 Ethics

The researchers will make a request to the ethical committee and all participants will have to give their written consent for their participation prior to the start of this study.

3.4 Intervention

For robotic rehabilitation, the ArmeoPower (AP) will be used in combination with the Manovo module to incorporate hand function. This is a robotic exoskeleton created for upper extremity rehabilitation. The patient's arm is placed on the exoskeleton and the AP provides anti-gravity support. The robot is connected to a screen where patients can see the progress they are making regarding the exercises. Rehabilitation can be provided in two modes, the active and the assistance mode. When the patient can move through the task actively the AP provides resistance. If the patient cannot execute the given task independently, the exoskeleton will assist the movement.

The participants will be allocated into two groups: the control group (CT) and the intervention group (IT). Both groups will receive similar interventions: one hour of target hitting exercises with the AP. For CT, these sessions will take place three times a week, while IT will have 5. The arm and hand with the most disability, established by the Upper Extremity Motor Score (UEMS) of the ASIA classification, will be trained throughout the intervention.

In the first therapy session, the participants will receive extensive instructions for the use and capabilities of the AP and the course of the intervention. All participants should start the first session in the assistance mode of the AP as an introduction to the device. Then, depending on their ability, training will continue in assistance or active mode. As their strength increases, upgrading to the active mode will be encouraged. During all therapy sessions, two therapists will be present to assist, coach and mentor the participants. Considering the current situation with COVID-19, the robot will be thoroughly disinfected between sessions by one of the therapists.

3.5 Outcome measures

We will use the Spinal Cord Independence Measure (SCIM III) to assess the functional status of the participants. To assess the muscle strength, the upper extremity motor score (UEMS) based on the ASIA classification will be used. To assess the fine and gross motor function on activity level, the researchers will use the Action Research Arm Test (ARAT). This study will assess the grip strength and pinch force using the JAMAR. The individual goals for each

participant will be determined by the Canadian Occupational Performance Measure (COPM). The foregoing outcome measures will be assessed at baseline, at half point (six weeks), after the intervention (12 weeks). Follow-up assessment will also be done at three and six months after the end of the intervention. All outcome measures will be ordered based on the International Classification of Functioning, Disability and Health (ICF).

3.5.1 Primary outcome measures

Our primary outcome measure will be the SCIM-III.

Activity level

The SCIM-III is a disability scale specifically designed for patients with SCI. The scale assesses different activities of daily living. It has three subscales: self-care, respiration and sphincter management and mobility. The total score is 100, a higher score indicates that a patient needs less aid to complete the task. The article of Itzkovich et al. (2007) showed that the SCIM-III is an efficient tool for functional assessment with SCI.

3.5.2 Secondary outcome measures

Functional level

To assess the muscle strength, the upper extremity motor score (UEMS) based on the ASIA classification will be used. The UEMS will be scored by the Manual Muscle Test (MMT) for elbow flexion and extension, wrist extension, third distal interphalangeal flexion, and fifth finger abduction. These are the five key muscle movements in C5 to T1. Each score was graded using the Medical Research Council (MRC) scale in accordance with ASIA guidelines (Kirshblum et al., 2011;Steeves et al., 2007).

The JAMAR dynamometer will be used for the assessment of grip strength, this is perceived as the golden standard. For the pinch force the pinch gauge of B&L engineering will be used (Mathiowetz, Weber, Volland, & Kashman, 1984).

After each therapy session, pain and perceived fatigue will be questioned, using the Visual Analogue Scale (VAS) and the BORG for fatigue, respectively.

Activity Level

The ARAT is a 19-item observational measure used to assess upper extremity performance (coordination, dexterity, and functioning) in stroke recovery, brain injury and multiple sclerosis. The test consists of four subscales: grasp, grip, pinch, and gross movement. Each item is scored on a four point scale where zero is 'no movement' and three is 'movement is performed normally'. Thus, a higher score correlates with a better performance. The total score of the ARAT is 57 (Pike, Lannin, Wales, & Cusick, 2018).

Participation level

The COPM will be used to determine the individual goals for each participant that they want to accomplish at the end of the intervention. Berardi et al. (2019) assessed the COPM as a reliable and valid measure for assessing SCI patients' perceived performance of daily activities and their satisfaction with their performance.

3.6 Data analysis

Descriptive statistics will be used to describe collection of information, sample size, and participants characteristics. Data-analyses will be performed using JMP statistical software. With this, normality will be checked from both groups. Both within-group evaluation and between group evaluations will be done to check whether the intervention has a significant effect compared to baseline measurements and if there is a significant difference between the two groups, and therefore whether frequency has an influence on functional outcomes. Mixed models analysis will be executed for both evaluations.

4. Time planning

The participants for this experimental study will be recruited between October 2021 and January 2021. Data will be gathered from February 2022 through April 2022. From May to June 2022 the obtained data will be analyzed, and the paper will be written.

5. References

Anderson, K. D. (2004, October). Targeting recovery: Priorities of the spinal cord-injured population. *Journal of Neurotrauma*. J Neurotrauma. https://doi.org/10.1089/neu.2004.21.1371

Berardi, A., Galeoto, G., Guarino, D., Marquez, M. A., De Santis, R., Valente, D., … Tofani, M. (2019). Construct validity, test-retest reliability, and the ability to detect change of the Canadian Occupational Performance Measure in a spinal cord injury population. *Spinal Cord Series and Cases*, *5*(1), 1–8. https://doi.org/10.1038/s41394-019-0196-6

Buehner, J. J., Forrest, G. F., Schmidt-Read, M., White, S., Tansey, K., & Basso, D. M. (2012). Relationship between ASIA examination and functional outcomes in the neurorecovery network locomotor training program. *Archives of Physical Medicine and Rehabilitation*, *93*(9), 1530–1540. https://doi.org/10.1016/j.apmr.2012.02.035

Cortes, M., Elder, J., Rykman, A., Murray, L., Avedissian, M., Stampa, A., … Edwards, D. J. (2013). Improved motor performance in chronic spinal cord injury following upper-limb robotic training. *NeuroRehabilitation*, *33*(1), 57–65. https://doi.org/10.3233/NRE-130928

de Leon, R., Hodgson, J. A., Roy, R. R., & Edgerton, V. R. (1994). Extensor- and flexor-like modulation within motor pools of the rat hindlimb during treadmill locomotion and swimming. *Brain Research*, *654*(2), 241–250. https://doi.org/10.1016/0006-8993(94)90485-5

Eng, D. P., Kadivar, Z., Sullivan, J. L., Pehlivan, A. U., O'Malley, M. K., Francisco, G. E., & Yozbatiran, N. (2011). Spatial and temporal movement characteristics after robotic training of arm and hand: A case study of a person with incomplete spinal cord injury (pp. 1711–1716). Institute of Electrical and Electronics Engineers (IEEE). https://doi.org/10.1109/iros.2011.6095134

Fehlings, M. G., Tetreault, L. A., Wilson, J. R., Kwon, B. K., Burns, A. S., Martin, A. R., … Harrop, J. S. (2017). A Clinical Practice Guideline for the Management of Acute Spinal Cord Injury: Introduction, Rationale, and Scope. https://doi.org/10.1177/2192568217703387

Francisco, G. E., Yozbatiran, N., Berliner, J., O'Malley, M. K., Pehlivan, A. U., Kadivar, Z., … Boake, C. (2017). Robot-Assisted Training of Arm and Hand Movement Shows Functional Improvements for Incomplete Cervical Spinal Cord Injury. *American Journal of Physical Medicine & Rehabilitation*, *96*(10), S171–S177. https://doi.org/10.1097/PHM.0000000000000815

Girgis, J., Merrett, D., Kirkland, S., Metz, G. A. S., Verge, V., Fouad, K., & Fouad, K. (2007). Reaching training in rats with spinal cord injury promotes plasticity and task specific recovery. https://doi.org/10.1093/brain/awm245

Hogan, N., Krebs, H. I., Rohrer, B., Palazzolo, J. J., Dipietro, L., Fasoli, S. E., … Volpe, B. T. (2006). Motions or muscles? Some behavioral factors underlying robotic assistance of motor recovery, *43*(5), 605–618. https://doi.org/10.1682/JRRD.2005.06.0103

Hwan Jung, J., Jin Lee, H., Youn Cho, D., Lim, J.-E., Suk Lee, B., Hyun Kwon, S., … Jeong Lee, S. (2019). Effects of Combined Upper Limb Robotic Therapy in Patients With Tetraplegic Spinal Cord Injury. *Annals of Rehabilitation Medicine Original Article Ann Rehabil Med*, *43*(4), 445–457. https://doi.org/10.5535/arm.2019.43.4.445

Itzkovich, M., Gelernter, I., Biering-Sorensen, F., Weeks, C., Laramee, M. T., Craven, B. C., … Catz, A. (2007). The Spinal Cord Independence Measure (SCIM) version III: Reliability and validity in a multi-center international study. *Disability and Rehabilitation*, *29*(24), 1926–1933. https://doi.org/10.1080/09638280601046302

Kang, Y., Ding, H., Zhou, H., Wei, Z., Liu, L., Pan, D., & Feng, S. (2017). Epidemiology of worldwide spinal cord injury: a literature review. *Journal of Neurorestoratology*, *Volume 6*, 1–9. https://doi.org/10.2147/jn.s143236

Kim, J., Lee, B. S., Lee, H. J., Kim, H. R., Cho, D. Y., Lim, J. E., … Han, Z. A. (2019). Clinical efficacy of upper limb robotic therapy in people with tetraplegia: a pilot randomized controlled trial. *Spinal Cord*, *57*(1), 49–57. https://doi.org/10.1038/s41393-018-0190-z

Kirshblum, S. C., Burns, S. P., Biering-Sorensen, F., Donovan, W., Graves, D. E., Jha, A., … Waring, W. (2011). International standards for neurological classification of spinal cord injury (Revised 2011). *Journal of Spinal Cord Medicine*. Taylor & Francis. https://doi.org/10.1179/204577211X13207446293695

Lang, C. E., Lohse, K. R., & Birkenmeier, R. L. (2015). Dose and timing in neurorehabilitation: Prescribing motor therapy after stroke. https://doi.org/10.1097/WCO.0000000000000256

Lu, Z., Tong, K. Y., Shin, H., Stampas, A., & Zhou, P. (2017). Robotic Hand-Assisted Training for Spinal Cord Injury Driven by Myoelectric Pattern Recognition: A Case Report. *American Journal of Physical Medicine &*

Rehabilitation, *96*(10), S146–S149. https://doi.org/10.1097/PHM.0000000000000798
Mathiowetz, V., Weber, K., Volland, G., & Kashman, N. (1984). Reliability and validity of grip and pinch strength evaluations. *Journal of Hand Surgery*, *9*(2), 222–226. https://doi.org/10.1016/S0363-5023(84)80146-X
Nam, K. Y., Kim, H. J., Kwon, S., Park, J.-W., Lee, H. J., & Yoo, A. (2017). Robot-assisted gait training (Lokomat) improves walking function and activity in people with spinal cord injury: a systematic review. https://doi.org/10.1186/s12984-017-0232-3
Pike, S., Lannin, N. A., Wales, K., & Cusick, A. (2018). A systematic review of the psychometric properties of the Action Research Arm Test in neurorehabilitation. *Australian Occupational Therapy Journal*, *65*(5), 449–471. https://doi.org/10.1111/1440-1630.12527
Sheperd Center. (2021). Spinal Cord Injury Types & Treatment | Shepherd Center. Retrieved June 3, 2021, from https://www.shepherd.org/patient-programs/spinal-cord-injury/about
Sledziewski, L., Schaaf, R. C., & Mount, J. (2012). Use of Robotics in Spinal Cord Injury: A Case Report. https://doi.org/10.5014/ajot.2012.000943
Steeves, J. D., Lammertse, D., Curt, A., Fawcett, J. W., Tuszynski, M. H., Ditunno, J. F., … Privat, A. (2007, March 30). Guidelines for the conduct of clinical trials for spinal cord injury (SCI) as developed by the ICCP panel: Clinical trial outcome measures. *Spinal Cord*. Spinal Cord. https://doi.org/10.1038/sj.sc.3102008
Vanmulken, D. A. M. M., Spooren, A. I. F., Bongers, H. M. H., & Seelen, H. A. M. (2015). Robot-assisted task-oriented upper extremity skill training in cervical spinal cord injury: A feasibility study. *Spinal Cord*, *53*(7), 547–551. https://doi.org/10.1038/sc.2014.250
Veerbeek, J. M., Van Wegen, E. E. H., Van Peppen, R. P. S., Hendriks, H. J. M., Rietberg, M. B., Van Der Wees, P. J., … Kwakkel, G. (2014). *KNGF-richtlijn Beroerte Praktijkrichtlijn*. Retrieved from www.fysionet-evidencebased.nl.
Volpe, B. T., Huerta, P. T., Zipse, J. L., Rykman, A., Edwards, D., Dipietro, L., … Krebs, I. (2009). *Robotic Devices as Therapeutic and Diagnostic Tools for Stroke Recovery*. *Arch Neurol* (Vol. 66). Retrieved from https://jamanetwork.com/
Zariffa, J., Kapadia, N., Kramer, J., Taylor, P., Alizadeh-Meghrazi, M., Zivanovic, V., … Steeves, J. D. (2012). Feasibility and efficacy of upper limb robotic rehabilitation in a subacute cervical spinal cord injury population. *Spinal Cord*, *50*, 220–226. https://doi.org/10.1038/sc.2011.104
Zbogar, D., Eng, J. J., Miller, W. C., Krassioukov, A. V, & Verrier, M. C. (2017). Movement repetitions in physical and occupational therapy during spinal cord injury rehabilitation. *Nature Publishing Group*, *55*, 172–179. https://doi.org/10.1038/sc.2016.129