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Highlighting Gaps in Spinal Cord Injury Research in Activity-based Interventions for the Upper Extremity: A Scoping Review

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Abstract

Background: Upper extremity activity-based therapy for neurologic disorders employs high-intensity, high repetition functional training to exploit neuroplasticity and improve function. Research focused on high-intensity upper extremity activity-based therapy for persons with spinal cord injury (SCI) is limited.

Objective: To summarize high-intensity activity-based interventions used in neurological disorders for their current or potential application to SCI.

Methods: The scoping review included articles from MEDLINE, CINAHL, Cochrane CENTRAL, and OTSeeker with the criteria: non-invasive activity-based interventions delivered atleast three times/week for two weeks, upper extremity functional outcomes, age 13 years or older, English language, and neurological disorders three months post onset/injury.

Results: The search yielded 172 studies. There were seven studies with SCI, all in adults. Activity-based interventions in SCI included task-specific training and gaming, with and without electrical stimulation, and a robotic exoskeleton. The other populations found in the review included studies in stroke, cerebral palsy, and multiple sclerosis. Thirty-four different interventions were reported in other populations. In comparison to the extensive stroke research, work in SCI was not found for high-intensity interventions using virtual reality, brain stimulation, rehabilitation devices, and applications to the home and telerehab settings.

Conclusion: The results highlight critical gaps within upper extremity high-intensity activity-based research in SCI.

Keywords: activity-based, high-intensity, rehabilitation, therapy, scoping review, upper extremity, neurological conditions, spinal cord injury

Article Type: Review Article

1. Introduction

Activity-based therapy for neurological conditions refers to rehabilitation interventions which aim to foster neurologic recovery through functional training characterized by high intensity and high repetition to take advantage of neuroplasticity (Roy et al., 2012; Hubbard et al., 2009; Winstein et al., 2014; Dromerick et al., 2006). Activity-based therapy for the upper extremity can include various protocols such as intense practice of routine activities, bimanual task training, task-specific training (e.g. purposeful, goal-directed novel tasks), functional activities or their components within virtual environments (e.g., virtual reality), and activities assisted by robots or exoskeletons. These functional activities can be enhanced by modalities such as electrical stimulation or neuromodulation. Activity-based therapy for the upper extremity has been used in rehabilitation for neurological conditions such as stroke (Kwakkel et al., 2008), spinal cord injury (SCI) (Roy et al., 2012; Jones et al., 2012), cerebral palsy (Brown et al., 2010), multiple sclerosis (Gatti et al., 2015), and Parkinson’s disease (Felix et al., 2012).

High-intensity protocols in SCI are essential to make gains in rehabilitation. Jones and colleagues (2012) highlighted three lower extremity clinical programs of activity-based therapy in SCI and summarized the evidence of their efficacy. Unfortunately, similar work is lacking in the area of upper extremity activity-based therapy. Backus (2008) in a seminal opinion piece, highlighted this overemphasis on locomotor training in SCI research despite the desire of persons with tetraplegia to improve arm and hand function to enhance their quality of life (Simpson ete al., 2012). The lack of guidance for clinicians and patients in designing upper extremity therapy programs is evident from a systematic review that summarized research in SCI from 1998 to

2009 (Backus et al., n.d). While this systematic review describing three SCI studies in upper extremity activity-based therapy was rigorous, it was not peer-reviewed. To our knowledge, no peer-reviewed publication has examined the literature beyond 2009.

Rehabilitation in inpatient settings can be structured to the high-intensity required to induce neuroplasticity via one-on-one therapy sessions (Whiteneck et al., 2011) . Beyond the first three months post-injury, neuroplasticity continues and high-intensity protocols continue to be needed (Roy et al., 2012). But after three months, many patients are no longer in inpatient settings where this can be easily achieved and only a few experience high-intensity programs to augment upper extremity recovery beyond that initial phase of rehabilitation. Moreover, since half of all spinal cord injuries result in incomplete tetraplegia (American Spinal Injury Association [ASIA], 2020), there is significant potential for recovery and reduced burden of care if high-intensity upper extremity strategies were available in the subacute and chronic phases. The best method for delivery of these types of protocols, with sufficient dosage, efficacy, and adherence is currently unknown yet extremely important to investigate. Research in activity-based therapy protocols in the subacute and chronic phases of SCI was thus of particular interest for this review.

Extensive research has been reported in activity-based rehabilitation for stroke with published systematic reviews (Kwakkel et al., 2008; Valkenborghs et al., 2019; Laver et al., 2017). Although neurological involvement in SCI differs from stroke, interventions based on principles of neuroplasticity and recovery have the potential to be effective in both conditions. Well-established evidence from stroke studies can guide SCI research in the immediate future with state-of-the-art equipment and devices (Backus, 2008). Similarly, it is important to review the evidence being generated for activity-based interventions in other conditions such as multiple sclerosis (Gatti et al., 2015) which may present with a combination of upper and lower motor neuron lesions and resultant dysfunction, similar to SCI.

Thus, the objective of this scoping review was to summarize the activity-based interventions used in neurological conditions for their current and potential application to subacute and chronic SCI. The scoping review methodology was chosen for this broad topic considering a large number of studies with varied designs and interventions. The scoping review also enabled a systematic search, screening, and extraction process with high-quality reporting using the Preferred Reporting of Items for Systematic Reviews and Meta-analyses (PRISMA)– scoping review extension (Tricco et al., 2018).

2. Methods

The scoping review protocol used the framework of Arksey and O'Malley (2005) with modifications by Levac and colleagues (2010) and was published (Thielen et al., 2018). The published protocol included multiple aims and the results of the primary aim are presented here, data for the secondary aims will be reported elsewhere. The methodology is briefly reviewed here and consisted of a five-step process: 1) framing the research questions, 2) searching and obtaining studies, 3) applying the eligibility criteria, 4) extracting and charting the data from a final set of studies, and 5) examining, summarizing, and reporting results.

2.1. Selection criteria

Eligibility criteria included: 1) English language, 2) peer-reviewed articles and dissertations, 3) from 2000 to 2016, 4) humans, 5) adults or adolescents, age 13 years or older, 6) three months or greater post-onset/injury, and 7) neurological diagnoses causing upper extremity motor impairments, 8) upper extremity activity-based therapy interventions with a frequency of at least three times/week and duration of at least two weeks, 9) upper extremity functional outcomes that require engagement in an activity. Autism and learning disabilities were excluded. Also excluded were mirror-based therapy and mental imagery that employ a mechanism different from movement-oriented activity-based therapy. Frequency and duration criteria were based on the definition of activity-based therapy that emphasizes protocols with substantial practice and repetition (Roy et al., 2012; Hubbard et al., 2009; Winstein et al., 2014). Children 13 years and older were included in this study since about 20% of spinal cord injuries occur in children and adolescents (ASIA, 2020) and research across the lifespan is needed. Also, teens may be ready to participate in clinical activity-based training protocols as compared to younger children who need play-based and parent-supported protocols. Since many studies in children younger than 13 may also include adolescents, the studies were included only if adolescent data was separately reported and could be extracted from the articles. The potential of the included interventions to individuals with SCI was considered in the planning of the selection criteria. Thus, constraint-induced movement therapy protocols as the main experimental intervention were excluded in this study since tetraplegia commonly presents with bilateral involvement and constraint of any one of the impaired upper extremities at a high intensity is undesirable. However, when constraint-induced movement therapy was one of the comparison groups in a randomized controlled trial, the studies were retained in the interest of the experimental activity-based intervention being evaluated.

2.2. Data Sources

The databases searched on Dec 22, 2016, and Dec 30, 2016, were: MEDLINE, CINAHL, Cochrane CENTRAL, and OT Seeker. A full search strategy for MEDLINE is included in Table 1. The data management software *Covidence* (www.covidence.org) was utilized and the librarian guided the research team on search terms, search strategy, data upload to *Covidence*, and setting up of the blinding for reviewers. Changes to the original protocol included no search of gray literature due to a large number of studies available from the databases.

2.3. Study Selection

All investigators and graduate students were trained by senior investigators. Two reviewers independently performed each stage of screening and extraction and a third reviewer provided consensus as needed. Final full-text articles were populated in *Covidence*.

2.4. Data Extraction and Synthesis

Data extraction templates were customized in *Covidence* with two guides: detailed instructions and brief reference. Regular team meetings were conducted to review the templates and clarify responses to ensure consensus. The following data was extracted, tabulated, and summarized by the research team: funding, country, population characteristics, study design, setting, technology, intervention, assessments, and outcomes. The following changes to the original protocol were made to facilitate improved extraction: i) outcomes focused closely on functional upper extremity measures; ii) dissertations published as journal articles were not duplicated; iii) studies on the same sample in two different papers were not duplicated. Data synthesis involved summarizing the data in tables based on the different types of interventions used in SCI and other neurological conditions to allow comparisons between the two populations.

3. Results

The database searches yielded 9465 studies. In total, 172 articles (2% of titles screened and 25% of full text screened) met the eligibility criteria. The study selection details are provided in the PRISMA diagram in Figure 1 and the PRISMA Scoping Review Statement was used for reporting (Tricco et al., 2018).

3.1. Studies in SCI

Table 2 shows the characteristics of the seven studies (Kowalczewski et al., 2011; Hoffman & Field-Fote, 2013; Szturm et al., 2008; Beekhuizen & Field-Fote, 2005, 2008; Yozbatiran et al., 2012; Spooren et al., 2011) found for upper extremity activity-based therapy in SCI. Studies varied in designs from randomized controlled trials to case studies and were conducted mainly in outpatient settings in North America, except for one study conducted in the home setting in Canada (Kowalczewski et al., 2011) and one in the Netherlands (Spooren et al., 2011). Five studies reported funding sources (Kowalczewski et al., 2011; Szturm et al., 2008; Beekhuizen & Field-Fote, 2005, 2008; Yozbatiran et al., 2012). The age range of the participants was from 22 to 70 years and included a total of 96 participants. The activity-based interventions included task-specific training with (n=3) (Hoffman & Field-Fote, 2013; Beekhuizen & Field-Fote, 2005,

2008) and without (n=1) (Spooren et al., 2011) electrical stimulation, gaming with (n=1) (Kowalczewski et al., 2011) and without (n=1) (Szturm et al., 2008) electrical stimulation, and a robotic exoskeleton (n=1) (Yozbatiran et al., 2012).

Table 3 shows the outcomes of the seven studies. Only one study used upper extremity functional measures relevant to SCI (Spooren et al., 2011) and no studies used patient-reported measures of upper extremity function. Follow-up data was reported in one study three months post-intervention (Spooren et al, 2011). The Jebsen Hand Function Test was the most commonly used upper extremity measure among the studies. For the upper extremity functional measures, all case studies reported improved scores (Yozbatiran et al., 2012; Szturm et al., 2008; Spooren et al, 2011). There were statistically significant improvements within the group for one non-randomized trial [26] (Spooren et al., 2011), and four randomized controlled trials (Kowalczewski et al., 2011; Hoffman & Field-Fote, 2013; Beekhuizen & Field-Fote, 2005, 2008). Significant between-group differences and notable gains were found in the randomized controlled trials focused on electrical stimulation combined with task-specific training (Hoffman & Field-Fote, 2013; Beekhuizen & Field-Fote, 2005, 2008) or gaming (Kowalczewski et al., 2011). Electrical stimulation has been used for functional training (Hoffman & Field-Fote, 2013) or priming (Beekhuizen & Field-Fote, 2005, 2008) in many of the studies. The intensity of the interventions ranged from 30 to 180 minutes a session, three to five times a week for three to eight weeks.

3.2. Studies in other neurological conditions

Table 2 shows the characteristics of the 165 studies found in other neurological conditions. The studies were primarily in stroke (n=157), and a few in cerebral palsy (n=3), multiple sclerosis (n=4), and mixed populations of stroke, multiple sclerosis, and brain tumor (n=1). Categorization of the different activity-based interventions yielded studies in task-specific training (n=70) (Woodbury et al., 2016), robot-assisted training (n=44) (Fluet et al., 2012), virtual reality (n=27) (Burdea et al., 2011), augmented reality (n=1) (Luo et al., 2005), mixed reality (n=4) (Colomer et al., 2016), and gaming (n=19) (Combs et al., 2012). Interventions were combined among themselves (Fluet et al., 2012) or enhanced by adding electrical stimulation (Hermann et al., 2010), priming (Kakuda et al., 2016), or rehabilitation devices (Galea et al., 2016). Telerehab was used in two task-specific training protocols (Benvenuti et al., 2014; Langan et al., 2013) and one virtual reality study (Piron et al., 2009). The setting for most studies was outpatient with other settings including inpatient, home, and mixed locations. Two studies included adolescents with cerebral palsy (Dinomais et al., 2013; Golomb et al., 2010).

Table 4 summarizes the outcomes and Appendix 1 provides further details. Thirty-four different interventions were found. The upper extremity functional outcomes were measured using performance-based and patient-reported measures. Statistically significant outcomes were reported within and between groups for various interventions and their combinations as shown in Table 4. The intensity of the interventions ranged from 30 to 360 minutes a session, 3 to 7 times a week for 2 to 12 weeks.

3.3. Comparisons between studies in SCI and other neurological conditions

Research in task-specific training, robot-assisted training, and gaming interventions were common among SCI and other neurological populations. Research in the SCI on high-intensity activity-based interventions was minimal. Studies in SCI frequently combined interventions with electrical stimulation. Gaming with electrical stimulation and rehab device was only noted for studies in SCI and was not found in other neurological conditions. Virtual reality and mixed reality interventions were not found in studies in SCI. Novel areas of research in other populations using brain stimulation, telerehab, augmented reality, music, subacute populations, and home settings were not found for SCI. Both populations lacked studies in optimal dosage, comparative effectiveness, and protocols for adolescents.

4. Discussion

The purpose of this scoping review was to summarize the high-intensity activity-based interventions used in neurological conditions for their current and potential application to SCI. The results indicate that SCI research is limited in this area with only seven studies through 2016. These findings indicate that there has been advancement in the field of SCI to fill the gaps highlighted in the literature (Backus, 2008) but are not sufficient to generate adequate evidence for the efficacy of activity-based interventions in SCI. The premise of intense and repetitive practice for neural reorganization or improvement is applicable across neurological conditions (Roy et al., 2012; Dromerick et al., 2006; Backus, 2008) and the activity-based interventions used in other neurological conditions could guide areas for potential research in SCI. The current gaps in SCI research and potential areas of investigation were illustrated by the findings, thus meeting the goals of this review.

The long-standing fallacy around spinal recovery ending at 6 to 12 months has recently been challenged by literature in cortical reorganization and spinal recovery (Filipp et al., 2019). Thus, the use of activity-based therapy in the subacute and chronic phases of SCI cannot be overemphasized. In particular, regaining upper extremity function is a priority for individuals with SCI and activity-based programs targeting the upper extremities are needed (Simpson et al., 2012). Activity-based programs in SCI for the upper extremity are more complex compared to the lower extremity programs due to the multiple degrees of freedom of the upper extremities, varied nature of tasks that people engage in, and limited research to support programming. This review points the researchers towards therapy programs that have been studied in other conditions such as stroke, multiple sclerosis, and cerebral palsy that can be examined for their effectiveness in SCI with appropriate modifications to meet their unique needs.

In this review, study protocols were found to often employ technology for activity-based therapy in various neurological populations. Technology has been leveraged to overcome barriers related to adherence for high-intensity protocols (King et al., 2021), support weak movements (Colomer et al., 2016), track outcomes in-person or remotely (Wittmann et al., 2016), and increase engagement (Friedman et al., 2014). Evidence is needed for SCI activity-based interventions that utilize technology and build on the work currently reported in the three studies using a robotic exoskeleton (Yozbatiran et al., 2012) and gaming (Kowalczewski et al., 2011; Szturm et al., 2008). Gaming with electrical stimulation was found to be an intervention of interest among the SCI studies since this intervention was not observed in other neurological conditions and may present a unique opportunity for future research (Kowalczewski et al., 2011). With many commercially available games, rehab devices, and virtual reality equipment, clinics are expanding the options they offer for rehabilitation in other neurological populations such as stroke. These options can be made available to individuals with SCI if evidence related to outcomes is generated by rigorous comparative effectiveness studies.

Adolescents experience six times greater incidence of SCI than children (Piatt & Imperato, 2018) and are developmentally and cognitively able to engage in activity-based therapy (Shierk et al., 2016) at a frequency and intensity comparable to adults without play-based interventions or parent-supported programs. This review neither found upper extremity studies in children where adolescent data was reported separately, nor studies where adolescents and adults were both included in the same trial, despite a high incidence of SCI in adolescents. Adolescents with SCI are in a transitional age where they may be ready for intense interventions designed for adults and their inclusion in adult clinical trials needs to be explored. Teens may find gaming and virtual reality interventions more appealing with the increased availability of accessible hardware and customizable options (Microsoft Corp, n.d.). A greater focus is needed for studies in adolescents with SCI where activity-based therapy can be leveraged during both the phases of subacute and chronic. However, there are known barriers to conducting research with adolescents, the primary is the separation of pediatric and adult health systems, limiting collaborations and thereby limiting research across transitional periods. Further, there are a few common outcome measures standardized for use with both adolescents and adults, which may restrict researchers from analyzing data across age groups or to transform the scores to derive meaning (Ni et al., 2019). Recently, studies have begun to create crosswalks between pediatric and adult measures (Slavin et al., 2016) and some measures are recommended as common data elements by the National Institute of Neurological Disorders and Stroke (e.g., PEDI-SCI)

(National Institute of Neurological Disorders and Stroke, n. d.), creating new ways to use advanced measures to address these barriers. Adolescents with SCI want to 'call the shots' (ASIA, 2020) and may benefit from programs designed for adults with SCI that are more self-driven versus those designed for young children that require parental support. Another challenge to adolescent research may be the lack of capability among researchers to recruit teens with SCI (Moreno et al., 2017), since individual institutions may or may not have registries for children with SCI. A centralized system such as the SCI Model Systems does not currently exist for adolescents, limiting the possibility of disseminating information about clinical trials and their results or the ability to track the outcomes of adolescents with SCI over their lifespan, further reducing the engagement of adolescents in clinical trials.

The demands of a high-intensity activity-based program can be justified for clients if relevant domains of patient-reported outcomes can be improved along with performance-based measures. Patient-reported outcomes of UE function are scales such as Capabilities of Upper Extremity Questionnaire or Spinal Cord Injury Functional Index domain of fine motor that ask about patient perceptions of difficulty. Performance-based measures on the other hand, are observer-reported measures of function while the rater instructs the patient to perform certain standardized tasks. Patient-reported measures allow gathering of information from patient's real-world use of their upper extremities, a highly desired outcome of activity-based therapy. The current study highlighted a gap in the reporting of patient-reported measures of upper extremity function within SCI studies. Only one SCI study used patient-reported outcomes (Spooren et al., 2011) when compared to many more studies in other populations, although not in all the trials in other populations. Patient-reported outcomes of upper extremity function (Moreno et al., 2017) add greater value to the measurement of rehabilitation outcomes and allow studies to be translated from research into clinical practice (Moura et al., 2016). The patient-reported measures of upper extremity function can be sensitive to changes in function in areas that are relevant to patients. Recent advances in the use of patient-reported measures need to be translated to the selection of measures for clinical trials in SCI. Another challenge in the SCI studies was the use of outcome measures that were not validated, such as the use of stroke-specific measures like the Wolf Motor Function Test (Beekhuizen & Fieldfote, 2005), and Chedoke Arm and Hand Activity Inventory (Szturm et al., 2008). There had been a dearth of functional outcomes for the upper extremity targeted to persons with tetraplegia, but that has changed in recent years (Marino et al., 2015; Marino et. al., 2018; Kalsi-Ryan, Beaton, et al., 2012; Kalsi-Ryan et al., 2019; Kalsi-Ryan, Curt, et al., 2012). Assessments such as the GRASSP and CUE-T have good reliability and responsiveness, and are beginning to appear at least as exploratory outcomes in clinical trials (ClinicalTrials.gov, 2019).

There is a need to develop unsupervised activity-based therapy interventions for clients to engage at home or through telerehab to develop high-intensity protocols that can be translated into the real-world. The pandemic of 2020 has further highlighted this need in urban areas whereas the need always existed in rural communities (Hale-Gallardo et al., 2020). The current review found only one home-based study in SCI and this presents an area of growth for activity-based therapy. Other neurological populations have also used protocols with mixed settings where primarily home-based protocols are enhanced by periodic booster sessions in the outpatient clinic (Page et al., 2016).

4.1. Limitations

The articles found in this scoping review were limited by the databases searched and the listings available within them. The exclusion of non-English publications, articles before the year 2000, or beyond 2017 further limited the scope of the literature. Thus, recent work in spine stimulation (Gad et al., 2018) was not included although they involved high intensity protocols (Inanici, et al., 2018). Gray literature databases were not searched but were included if found through other sources such as dissertations found through CINAHL database. The activity-based therapy interventions reviewed were highly varied, and the categorizations presented here may not adequately capture the complexity of some interventions. Another limitation is in the currently available research in other populations, which although helpful to highlight the potential areas of growth for SCI research, itself has deficiencies; and the results should be interpreted in consideration of this drawback.

4.2. Conclusion

The findings of this review highlight gaps in high-intensity upper extremity activity-based therapy research in SCI. Future research studies can focus on key areas of growth such as a focus on adolescents, home or telerehab protocols, comparative effectiveness studies, use of relevant outcome measures, and exploration of interventions established in other neurological conditions such as virtual reality, rehabilitation devices, and brain stimulation.

Declaration of Interest

None declared

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Table 1. Search Strategy for MEDLINE

Database(s): Ovid MEDLINE(R), Ovid MEDLINE(R) Daily, Epub Ahead of Print, and In-Process & Other Non-Indexed Citations

Sequence	Searches
1	exp Spinal Cord Injuries/
2	spinal cord injur*.ti,ab.
3	exp Spinal Cord Diseases/
4	spinal cord dysfunction.ti,ab.
5	exp Stroke/
6	stroke.ti,ab.
7	strokes.ti,ab.
8	cerebral vascular accident*.ti,ab.
9	exp Brain Injuries/
10	brain injur*.ti,ab.
11	Cerebral Palsy/
12	cerebral palsy.ti,ab.
13	exp Multiple Sclerosis/
14	multiple sclerosis.ti,ab.
15	amyotrophic lateral sclerosis.ti,ab.
16	Quadriplegia/
17	quadripleg*.ti,ab.
18	quadripare*.ti,ab.
19	or/1-18
20	exp Upper Extremity/
21	(upper adj3 (limb or extremity)).ti,ab,sh,kf.
22	(arm or shoulder or elbow or forearm or (hand not ("on the other hand" or "hand search*")) or wrist or finger or fingers).ti,ab,sh,kf.
23	or/20-22
24	23 and 19
25	Activity based.ti,ab.
26	((repetitive or specific) adj3 task adj3 (training or practice)).ti,ab.
27	Neurological Rehabilitation/
28	Neurorehabilitation.ti,ab.
29	rehabilitation.ti,kf,fs.
30	(reach* not (reach* adj2 statistical*)).ti,ab,kf.
31	grasp*.ti,ab,kf.
32	prehensi*.ti,ab,kf.
33	or/25-32
34	24 and 33
35	Animals/ not Humans/
36	34 not 35
37	limit 36 to english
38	limit 37 to yr="2000 -Current"
39	remove duplicates from 38

Table 2. Characteristics of Included Studies

Characteristics	Spinal Cord Injury	Other Neurological Conditions
Number of studies	7	165 (stroke, 157; cerebral palsy, 3; multiple sclerosis, 4; mixed, 1)
Year of Publication		
2001 to 2005	1	15
2006 to 2011	4	53
2012 to 2017	2	97
Continent (Countries)		
North America (United States and Canada)	6	79
Europe (Belgium, Finland, France, Germany, Ireland, Italy, Netherlands, Portugal, Spain, Sweden, Switzerland, United Kingdom)	1	39
Asia (China, India, Israel, Japan, Jordan, Pakistan, South Korea, Taiwan, Thailand)	-	35
Oceania (Australia and New Zealand)	-	8
South America (Brazil)	-	3
Intercontinental (United States and South Korea)	-	1
Funding Source		
Funded	4	130
Not reported	2	23
Not funded	1	12
Time Post Injury/Onset		
Chronic (> 6 months)	7	142
Subacute (3 to 6 months)	-	23
Study Designs*		
Randomized Controlled Trials	4	84
Non-randomized/One-Group	2	43
Case series/Case studies	1	38
Settings		
Outpatient	6	106
Home	1	27
Mixed	-	14
Inpatient	-	15
Unclear/Not Reported	-	3
Interventions		
Task Specific Training		
• Not combined with other interventions	1	31
• With electrical stimulation for training	1	16
• With electrical stimulation for priming	2	4
• With electrical stimulation and rehab device	-	1
• With electrical stimulation, rehab device, gaming	-	1
• With brain stimulation for priming	-	8
• With rehab device	-	5
• With metronome	-	1
• With musical keyboard	-	1
• With telerehab	-	2
Robot-assisted training	-	20
• With electrical stimulation for training	-	2
• With rehab Device	-	1
• With task-specific training	-	9
• With exoskeleton-orthosis	1	6
• With exoskeleton-orthosis and TST	-	5
• With VR	-	1
Virtual Reality		
• Not combined with other interventions	-	12
• With brain stimulation for priming	-	2
• With conventional therapy	-	2
• With rehab device	-	8
• With robot	-	2

• With telerehab	-	1
Augmented reality with exoskeleton-orthosis	-	1
Gaming		
• Not combined with other interventions	1	10
• With electrical stimulation and rehab device	1	-
• With priming task	-	1
• With rehab device	-	5
• With task-specific training and rehab device	-	1
• With dynamic orthosis	-	2
Mixed Reality	-	4

Note:*Definitions of study designs: Case studies/series includes research designs with descriptive reporting of data at two or more time points and do not include any group level inferential statistics; Non-randomized/One Group includes research designs with one or more groups with no randomization and include group level inferential statistics; Randomized controlled trials includes research designs where two or more groups/conditions are randomized to different interventions and results include within and/or between group inferential statistics.

Table 3. Interventions and Outcomes of Spinal Cord Injury Studies

Study	Interventions	Setting	Study Design	Sample Size	ASIA Grade	Measures	Within Group Results	Between Group Results
Task-specific Training without Electrical Stimulation (30 minutes, x3/week, 8 weeks)								
Spooren et al., 2011	TST receiving active rehab (EXP1) vs TST post rehab (EXP2) vs CT (CON)	Outpatient	Non-randomized: 3 Group	12, 11, 11	A to D	GAS, COPM, VLT	Positive in EXP1 and EXP2 at post and 3 mon f/u.	NR
						VLT	Positive in EXP1 at discharge. Positive in EXP1 and EXP2 at post and 3 mon f/u.	No statistical difference
						FIM, QIF	Positive in EXP1 and CON at discharge. No statistical difference in EXP1 and EXP2 at post and 3 mon f/u.	No statistical difference
Task-specific Training with Electrical Stimulation for Priming (120 minutes, x5/week, 3 weeks)								
Beekhuizen et al., 2005	TST with Nerve stimulation (EXP) vs TST (CON)	Outpatient	RCT: Parallel: 2 Group	5, 5	C and D	WMFT, Pinch	Positive for EXP	Positive, EXP did better than CON
						JHFT	Positive both groups	Positive, EXP did better than CON
Beekhuizen et al., 2008	TST with Nerve Stimulation (EXP1) vs TST (EXP2) vs Somatosensory Stimulation (EXP3) vs No Active (CON)	Outpatient	RCT: Parallel: 4 Group	6, 6, 6, 6	C and D	JHFT	Positive in EXP1, EXP2, EXP3	Positive, EXP1 and EXP3 did better than CON
						WMFT, Pinch	Positive in EXP1 and EXP3	Positive, EXP1 and EXP3 did better than CON
Task Specific Training with Electrical Stimulation for Training (120 minutes, x5/week, 3 weeks)								
Hoffman et al., 2013	Somatosensory/FES with unimanual/bimanual training (EXP) vs No Active Delayed (CON)	Outpatient	RCT: Parallel: 2 Group	10, 9	A to D	JHFT	Positive in both groups	Positive, EXP did better than CON
Robot-assisted training with exoskeleton-orthosis (180 minutes, x3/week, 3 weeks)								
Yozbatiran et al., 2012	Robotic Exoskeleton	Outpatient	Case Study	1	C	JHFT, ARAT	Improved scores	N/A
Gaming (60 minutes, x3/week, 5 weeks)								
Szturm et al., 2008	Gaming with object manipulation	Outpatient	Case Study	1	NR (Incomplete injury)	JHFT	Improved scores	N/A
						CAHAI, Pinch	No difference	No difference
Gaming with Electrical Stimulation and Rehab Device (60 minutes, x5/week, 6 weeks)								
Kowalczewski et al., 2011	Gaming with FES (EXP) vs CT with Electrical stimulation (CON)	Home	RCT: Crossover	9, 9	A to D	ARAT, Grip	Positive for both groups at post	Positive, EXP did better than CON at post
						Grip	Positive for EXP at post	No statistical difference
						Pinch	No statistical difference	No statistical difference

Abbreviations: ***ARAT***=Action Research Arm Test, ***CAHAI***=Chedoke Arm and Hand Activity Inventory, ***CON***=Control group/condition, ***COPM***=Canadian Occupational Performance Measure, ***CT***=Conventional Therapy, ***EXP***=Experimental group/condition, ***FES***=Functional Electrical Stimulation, ***FIM***=Functional Independence Measure, ***GAS***=Goal Attainment Scale, ***Grip***=Grip Dynamometry, ***JHFT***=Jebsen Hand Function Test, ***N/A***=Not Applicable, ***Positive***=Statistically significant difference on group level inferential statistics, ***QIF***=Quadriplegia Index of Function, ***RCT***=Randomized Controlled Trial, ***TST***=Task-specific training, ***VLT***=Van Lieshout Test, ***WMFT***=Wolf Motor Function Test.

Table 4. Interventions and Outcomes of Studies in Other Neurological Conditions

Intervention	Total number of studies	Number of studies with statistically significant within-group improvement	Number of studies with statistically significant between-group improvement	Number of studies using patient-reported outcome measures of upper extremity function	Intensity
Task Specific Training - overall	**70**	**45 at posttest 9 at follow-up**	**24 at posttest 2 at follow-up**	**27**	**30 to 280 min 2 to 7 days/wk 2 to 12 wks**
• Not combined with another intervention	31	21 at posttest 2 at follow-up	12 at posttest 1 at follow-up	14	30 to 240 min 2 to 7 days/wk 2 to 10 wks
• With electrical stimulation for training	16	7 at posttest 3 at follow-up	3 at posttest	6	30 to 180 min 3 to 7 days/wk 2 to 12 wks
• With electrical stimulation for priming	4	4 at posttest 2 at follow-up	3 at posttest 1 at follow-up	2	60 to 360 min 3 to 5 days/wk 2 to 4 wks
• With electrical stimulation and rehab device	1	1 at posttest	1 at posttest	-	60 min 3 days/wk 4 wks
• With electrical stimulation, rehab device, gaming	1	1 at posttest	-	-	60 min 5 days/wk 6 wks
• With brain stimulation for priming	8	6 at posttest 2 at follow-up	2 at posttest	1	75 to 300 min 4 to 6 days/wk 2 to 4 wks
• With rehab device	5	4 at posttest	2 at posttest	1	30 to 60 min 3 to 5 days/wk 3 to 12 wks
• With metronome	1	-	-	1	60 min 3 days/wk 4 wks
• With musical keyboard	1	1 at posttest	-	1	90 min 5 days/wk 3 wks
• With telerehab	2	-	1 at posttest	1	60 min 4 to 5 days/wk 6 to 12 wks
Robot-assisted training - overall	**44**	**27 at posttest 15 at follow-up**	**17 at posttest 5 at follow-up**	**21**	**30 to 300 min 3 to 7 days/wk 2 to 10 wks**
• Not combined with another intervention	20	10 at posttest 6 at follow-up	10 at posttest 2 at follow-up	11	30 to 180 min 3 to 7 days/wk 3 to 12 wks
• With electrical stimulation for training	2	2 at posttest	1 at posttest	1	30 to 90 min 4 to 5 days/wk 4 to 5 wks
• With rehab Device	1	1 at posttest 1 at follow-up	-	-	165 min 4 days/wk 2 wks
• With task-specific training	9	4 at posttest 2 at follow-up	2 at posttest 1 at follow-up	5	60 to 300 min 3 to 5 days/wk 3 to 12 wks
• With exoskeleton-orthosis	6	4 at posttest 3 at follow-up	2 at posttest 1 at follow-up	2	30 to 90 min 3 days/wk 4 to 12 wks
• With exoskeleton-orthosis and TST	5	5 at post-test 2 at follow-up	1 at posttest 1 at follow-up	1	30 to 90 min 3 days/wk 4 to 12 wks
• With VR	1	1 at posttest 1 at follow-up	1 at posttest	1	90 min 5 days/wk 3 wks

Virtual Reality	**27**	**11 at posttest** **1 at follow-up**	**5 at posttest** **1 at follow up**	**7**	30 to 300 min 3 to 7 days/wk 2 to 8 wks
• Not combined with another intervention	12	3 at posttest	2 at posttest	5	30 to 120 min 3 to 7 days/wk 2 to 8 wks
• With brain stimulation for priming	2	2 at posttest	1 at posttest	1	30 to 60 min 3 to 5 days/wk 3 to 5 wks
• With conventional therapy	2	2 at posttest	1 at posttest	-	60 to 120 min 5 days/wk 4 wks
• With rehab device	8	2 at posttest 1 at follow-up	1 at posttest 1 at follow-up	1	45 to 300 min 3 to 5 days/wk 2 to 6 wks
• With robot	2	1 at posttest		-	60 to 75 min 3 days/wk 2 to 4 wks
• With telerehab	1	1 at posttest	1 at posttest		60 min 5 days/wk 4 wks
Augmented reality with exoskeleton-orthosis	**1**	**-**	**-**	**-**	30 min 3 days/wk 6 wks
Mixed Reality	**4**	**4 at posttest** **1 at follow-up**	**2 at posttest**	**1**	45 to 120 min 3 to 5 days/wk 4 to 8 wks
Gaming	**19**	**12 at posttest** **10 at follow-up**	**1 at posttest** **4 at follow-up**	**10**	20 to 165 min 3 to 6 days/wk 2 to 12 wks
• Not combined with another intervention	10	5 at posttest 5 at follow-up	1 at posttest 2 at follow-up	7	30 to 60 min 3 to 6 days/wk 2 to 9 wks
• With priming task	1	-	-	1	165 min 5 days/wk 2 wks
• With rehab device	5	4 at posttest 2 at follow-up	2 at follow-up	1	20 to 165 min 3 to 5 days/wk 2 to 12 wks
• With task-specific training and rehab device	1	1 at posttest 1 at follow-up	-	-	150 min 5 days/wk 3 wks
• With orthosis	2	2 at posttest 2 at follow-up	-	1	30 min 6 days/wk 6 wks

Abbreviations: ***min***, minutes ***wk,*** week

Figure Captions

Figure 1. Study Selection PRISMA Flow Diagram for the Scoping Review. ***mon***, months; ***n***, number of articles; ***PRISMA***, Preferred Reporting Items of Systematic Reviews and Meta-analyses

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