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

3

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21

22

23 **Abstract**

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

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

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

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

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

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

45 **Article Type:** Review Article

46 1. Introduction

47

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

60

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

69 2009 (Backus et al., n.d). While this systematic review describing three SCI studies in upper
70 extremity activity-based therapy was rigorous, it was not peer-reviewed. To our knowledge, no
71 peer-reviewed publication has examined the literature beyond 2009.

72

73 Rehabilitation in inpatient settings can be structured to the high-intensity required to induce
74 neuroplasticity via one-on-one therapy sessions (Whiteneck et al., 2011) . Beyond the first three
75 months post-injury, neuroplasticity continues and high-intensity protocols continue to be needed
76 (Roy et al., 2012). But after three months, many patients are no longer in inpatient settings where
77 this can be easily achieved and only a few experience high-intensity programs to augment upper
78 extremity recovery beyond that initial phase of rehabilitation. Moreover, since half of all spinal
79 cord injuries result in incomplete tetraplegia (American Spinal Injury Association [ASIA],
80 2020), there is significant potential for recovery and reduced burden of care if high-intensity
81 upper extremity strategies were available in the subacute and chronic phases. The best method
82 for delivery of these types of protocols, with sufficient dosage, efficacy, and adherence is
83 currently unknown yet extremely important to investigate. Research in activity-based therapy
84 protocols in the subacute and chronic phases of SCI was thus of particular interest for this
85 review.

86

87 Extensive research has been reported in activity-based rehabilitation for stroke with published
88 systematic reviews (Kwakkel et al., 2008; Valkenborghs et al., 2019; Laver et al., 2017).

89 Although neurological involvement in SCI differs from stroke, interventions based on principles
90 of neuroplasticity and recovery have the potential to be effective in both conditions. Well-
91 established evidence from stroke studies can guide SCI research in the immediate future with

92 state-of-the-art equipment and devices (Backus, 2008). Similarly, it is important to review the
93 evidence being generated for activity-based interventions in other conditions such as multiple
94 sclerosis (Gatti et al., 2015) which may present with a combination of upper and lower motor
95 neuron lesions and resultant dysfunction, similar to SCI.

96

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

104

105 **2. Methods**

106

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

114

115 *2.1. Selection criteria*

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

137 the studies were retained in the interest of the experimental activity-based intervention being
138 evaluated.

139

140 **2.2. Data Sources**

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

147

148 **2.3. Study Selection**

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

152

153 **2.4. Data Extraction and Synthesis**

154 Data extraction templates were customized in *Covidence* with two guides: detailed instructions
155 and brief reference. Regular team meetings were conducted to review the templates and clarify
156 responses to ensure consensus. The following data was extracted, tabulated, and summarized by
157 the research team: funding, country, population characteristics, study design, setting, technology,
158 intervention, assessments, and outcomes. The following changes to the original protocol were
159 made to facilitate improved extraction: i) outcomes focused closely on functional upper

160 extremity measures; ii) dissertations published as journal articles were not duplicated; iii) studies
161 on the same sample in two different papers were not duplicated. Data synthesis involved
162 summarizing the data in tables based on the different types of interventions used in SCI and other
163 neurological conditions to allow comparisons between the two populations.

164

165 **3. Results**

166

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

171

172 ***3.1. Studies in SCI***

173 Table 2 shows the characteristics of the seven studies (Kowalczewski et al., 2011; Hoffman &
174 Field-Fote, 2013; Szturm et al., 2008; Beekhuizen & Field-Fote, 2005, 2008; Yozbatiran et al.,
175 2012; Spooren et al., 2011) found for upper extremity activity-based therapy in SCI. Studies
176 varied in designs from randomized controlled trials to case studies and were conducted mainly in
177 outpatient settings in North America, except for one study conducted in the home setting in
178 Canada (Kowalczewski et al., 2011) and one in the Netherlands (Spooren et al., 2011). Five
179 studies reported funding sources (Kowalczewski et al., 2011; Szturm et al., 2008; Beekhuizen &
180 Field-Fote, 2005, 2008; Yozbatiran et al., 2012). The age range of the participants was from 22
181 to 70 years and included a total of 96 participants. The activity-based interventions included
182 task-specific training with (n=3) (Hoffman & Field-Fote, 2013; Beekhuizen & Field-Fote, 2005,

183 2008) and without (n=1) (Spooren et al., 2011) electrical stimulation, gaming with (n=1)
184 (Kowalczewski et al., 2011) and without (n=1) (Szturm et al., 2008) electrical stimulation, and a
185 robotic exoskeleton (n=1) (Yozbatiran et al., 2012).

186

187 Table 3 shows the outcomes of the seven studies. Only one study used upper extremity
188 functional measures relevant to SCI (Spooren et al., 2011) and no studies used patient-reported
189 measures of upper extremity function. Follow-up data was reported in one study three months
190 post-intervention (Spooren et al., 2011). The Jebsen Hand Function Test was the most commonly
191 used upper extremity measure among the studies. For the upper extremity functional measures,
192 all case studies reported improved scores (Yozbatiran et al., 2012; Szturm et al., 2008; Spooren
193 et al., 2011). There were statistically significant improvements within the group for one non-
194 randomized trial [26] (Spooren et al., 2011), and four randomized controlled trials
195 (Kowalczewski et al., 2011; Hoffman & Field-Fote, 2013; Beekhuizen & Field-Fote, 2005,
196 2008). Significant between-group differences and notable gains were found in the randomized
197 controlled trials focused on electrical stimulation combined with task-specific training (Hoffman
198 & Field-Fote, 2013; Beekhuizen & Field-Fote, 2005, 2008) or gaming (Kowalczewski et al.,
199 2011). Electrical stimulation has been used for functional training (Hoffman & Field-Fote, 2013)
200 or priming (Beekhuizen & Field-Fote, 2005, 2008) in many of the studies. The intensity of the
201 interventions ranged from 30 to 180 minutes a session, three to five times a week for three to
202 eight weeks.

203

204 ***3.2. Studies in other neurological conditions***

205 Table 2 shows the characteristics of the 165 studies found in other neurological conditions. The
206 studies were primarily in stroke (n=157), and a few in cerebral palsy (n=3), multiple sclerosis
207 (n=4), and mixed populations of stroke, multiple sclerosis, and brain tumor (n=1). Categorization
208 of the different activity-based interventions yielded studies in task-specific training (n=70)
209 (Woodbury et al., 2016), robot-assisted training (n=44) (Fluet et al., 2012), virtual reality (n=27)
210 (Burdea et al., 2011), augmented reality (n=1) (Luo et al., 2005), mixed reality (n=4) (Colomer et
211 al., 2016), and gaming (n=19) (Combs et al., 2012). Interventions were combined among
212 themselves (Fluet et al., 2012) or enhanced by adding electrical stimulation (Hermann et al.,
213 2010), priming (Kakuda et al., 2016), or rehabilitation devices (Galea et al., 2016). Telerehab
214 was used in two task-specific training protocols (Benvenuti et al., 2014; Langan et al., 2013) and
215 one virtual reality study (Piron et al., 2009). The setting for most studies was outpatient with
216 other settings including inpatient, home, and mixed locations. Two studies included adolescents
217 with cerebral palsy (Dinomais et al., 2013; Golomb et al., 2010).

218
219 Table 4 summarizes the outcomes and Appendix 1 provides further details. Thirty-four different
220 interventions were found. The upper extremity functional outcomes were measured using
221 performance-based and patient-reported measures. Statistically significant outcomes were
222 reported within and between groups for various interventions and their combinations as shown in
223 Table 4. The intensity of the interventions ranged from 30 to 360 minutes a session, 3 to 7 times
224 a week for 2 to 12 weeks.

225

226 ***3.3. Comparisons between studies in SCI and other neurological conditions***

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

236

237 **4. Discussion**

238 The purpose of this scoping review was to summarize the high-intensity activity-based
239 interventions used in neurological conditions for their current and potential application to SCI.
240 The results indicate that SCI research is limited in this area with only seven studies through
241 2016. These findings indicate that there has been advancement in the field of SCI to fill the gaps
242 highlighted in the literature (Backus, 2008) but are not sufficient to generate adequate evidence
243 for the efficacy of activity-based interventions in SCI. The premise of intense and repetitive
244 practice for neural reorganization or improvement is applicable across neurological conditions
245 (Roy et al., 2012; Dromerick et al., 2006; Backus, 2008) and the activity-based interventions
246 used in other neurological conditions could guide areas for potential research in SCI. The current
247 gaps in SCI research and potential areas of investigation were illustrated by the findings, thus
248 meeting the goals of this review.

249

250 The long-standing fallacy around spinal recovery ending at 6 to 12 months has recently been
251 challenged by literature in cortical reorganization and spinal recovery (Filipp et al., 2019). Thus,
252 the use of activity-based therapy in the subacute and chronic phases of SCI cannot be
253 overemphasized. In particular, regaining upper extremity function is a priority for individuals
254 with SCI and activity-based programs targeting the upper extremities are needed (Simpson et al.,
255 2012). Activity-based programs in SCI for the upper extremity are more complex compared to
256 the lower extremity programs due to the multiple degrees of freedom of the upper extremities,
257 varied nature of tasks that people engage in, and limited research to support programming. This
258 review points the researchers towards therapy programs that have been studied in other
259 conditions such as stroke, multiple sclerosis, and cerebral palsy that can be examined for their
260 effectiveness in SCI with appropriate modifications to meet their unique needs.

261
262 In this review, study protocols were found to often employ technology for activity-based therapy
263 in various neurological populations. Technology has been leveraged to overcome barriers related
264 to adherence for high-intensity protocols (King et al., 2021), support weak movements (Colomer
265 et al., 2016), track outcomes in-person or remotely (Wittmann et al., 2016), and increase
266 engagement (Friedman et al., 2014). Evidence is needed for SCI activity-based interventions that
267 utilize technology and build on the work currently reported in the three studies using a robotic
268 exoskeleton (Yozbatiran et al., 2012) and gaming (Kowalczewski et al., 2011; Szturm et al.,
269 2008). Gaming with electrical stimulation was found to be an intervention of interest among the
270 SCI studies since this intervention was not observed in other neurological conditions and may
271 present a unique opportunity for future research (Kowalczewski et al., 2011). With many
272 commercially available games, rehab devices, and virtual reality equipment, clinics are

273 expanding the options they offer for rehabilitation in other neurological populations such as
274 stroke. These options can be made available to individuals with SCI if evidence related to
275 outcomes is generated by rigorous comparative effectiveness studies.

276
277 Adolescents experience six times greater incidence of SCI than children (Piatt & Imperato, 2018)
278 and are developmentally and cognitively able to engage in activity-based therapy (Shierk et al.,
279 2016) at a frequency and intensity comparable to adults without play-based interventions or
280 parent-supported programs. This review neither found upper extremity studies in children where
281 adolescent data was reported separately, nor studies where adolescents and adults were both
282 included in the same trial, despite a high incidence of SCI in adolescents. Adolescents with SCI
283 are in a transitional age where they may be ready for intense interventions designed for adults
284 and their inclusion in adult clinical trials needs to be explored. Teens may find gaming and
285 virtual reality interventions more appealing with the increased availability of accessible hardware
286 and customizable options (Microsoft Corp, n.d.). A greater focus is needed for studies in
287 adolescents with SCI where activity-based therapy can be leveraged during both the phases of
288 subacute and chronic. However, there are known barriers to conducting research with
289 adolescents, the primary is the separation of pediatric and adult health systems, limiting
290 collaborations and thereby limiting research across transitional periods. Further, there are a few
291 common outcome measures standardized for use with both adolescents and adults, which may
292 restrict researchers from analyzing data across age groups or to transform the scores to derive
293 meaning (Ni et al., 2019). Recently, studies have begun to create crosswalks between pediatric
294 and adult measures (Slavin et al., 2016) and some measures are recommended as common data
295 elements by the National Institute of Neurological Disorders and Stroke (e.g., PEDI-SCI)

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

306
307 The demands of a high-intensity activity-based program can be justified for clients if relevant
308 domains of patient-reported outcomes can be improved along with performance-based measures.
309 Patient-reported outcomes of UE function are scales such as Capabilities of Upper Extremity
310 Questionnaire or Spinal Cord Injury Functional Index domain of fine motor that ask about
311 patient perceptions of difficulty. Performance-based measures on the other hand, are observer-
312 reported measures of function while the rater instructs the patient to perform certain standardized
313 tasks. Patient-reported measures allow gathering of information from patient’s real-world use of
314 their upper extremities, a highly desired outcome of activity-based therapy. The current study
315 highlighted a gap in the reporting of patient-reported measures of upper extremity function
316 within SCI studies. Only one SCI study used patient-reported outcomes (Spooren et al., 2011)
317 when compared to many more studies in other populations, although not in all the trials in other
318 populations. Patient-reported outcomes of upper extremity function (Moreno et al., 2017) add

319 greater value to the measurement of rehabilitation outcomes and allow studies to be translated
320 from research into clinical practice (Moura et al., 2016). The patient-reported measures of upper
321 extremity function can be sensitive to changes in function in areas that are relevant to patients.
322 Recent advances in the use of patient-reported measures need to be translated to the selection of
323 measures for clinical trials in SCI. Another challenge in the SCI studies was the use of outcome
324 measures that were not validated, such as the use of stroke-specific measures like the Wolf
325 Motor Function Test (Beekhuizen & Fieldfote, 2005), and Chedoke Arm and Hand Activity
326 Inventory (Szturm et al., 2008). There had been a dearth of functional outcomes for the upper
327 extremity targeted to persons with tetraplegia, but that has changed in recent years (Marino et al.,
328 2015; Marino et. al., 2018; Kalsi-Ryan, Beaton, et al., 2012; Kalsi-Ryan et al., 2019; Kalsi-Ryan,
329 Curt, et al., 2012). Assessments such as the GRASSP and CUE-T have good reliability and
330 responsiveness, and are beginning to appear at least as exploratory outcomes in clinical trials
331 (ClinicalTrials.gov, 2019).

332
333 There is a need to develop unsupervised activity-based therapy interventions for clients to
334 engage at home or through telerehab to develop high-intensity protocols that can be translated
335 into the real-world. The pandemic of 2020 has further highlighted this need in urban areas
336 whereas the need always existed in rural communities (Hale-Gallardo et al., 2020). The current
337 review found only one home-based study in SCI and this presents an area of growth for activity-
338 based therapy. Other neurological populations have also used protocols with mixed settings
339 where primarily home-based protocols are enhanced by periodic booster sessions in the
340 outpatient clinic (Page et al., 2016).

341

342 ***4.1. Limitations***

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

354

355 ***4.2. Conclusion***

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

361 **Declaration of Interest**

362 None declared

363

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369

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625
626

627 **Table 1. Search Strategy for MEDLINE**

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

630 **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

631 Note:*Definitions of study designs: Case studies/series includes research designs with descriptive reporting of data at two or more time points
632 and do not include any group level inferential statistics; Non-randomized/One Group includes research designs with one or more groups with no
633 randomization and include group level inferential statistics; Randomized controlled trials includes research designs where two or more
634 groups/conditions are randomized to different interventions and results include within and/or between group inferential statistics.
635

636
637**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)								
Sporeen 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 VLT FIM, QIF	Positive in EXP1 and EXP2 at post and 3 mon f/u. Positive in EXP1 at discharge. Positive in EXP1 and EXP2 at post and 3 mon f/u. Positive in EXP1 and CON at discharge. No statistical difference in EXP1 and EXP2 at post and 3 mon f/u.	NR No statistical difference 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 JHFT	Positive for EXP Positive both groups	Positive, EXP did better than CON 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 WMFT, Pinch	Positive in EXP1, EXP2, EXP3 Positive in EXP1 and EXP3	Positive, EXP1 and EXP3 did better than CON 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 CAHAI, Pinch	Improved scores No difference	N/A 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 Grip Pinch	Positive for both groups at post Positive for EXP at post No statistical difference	Positive, EXP did better than CON at post No statistical difference No statistical difference

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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.

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

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647Abbreviations: *min*, minutes *wk*, week

648 **Figure Captions**

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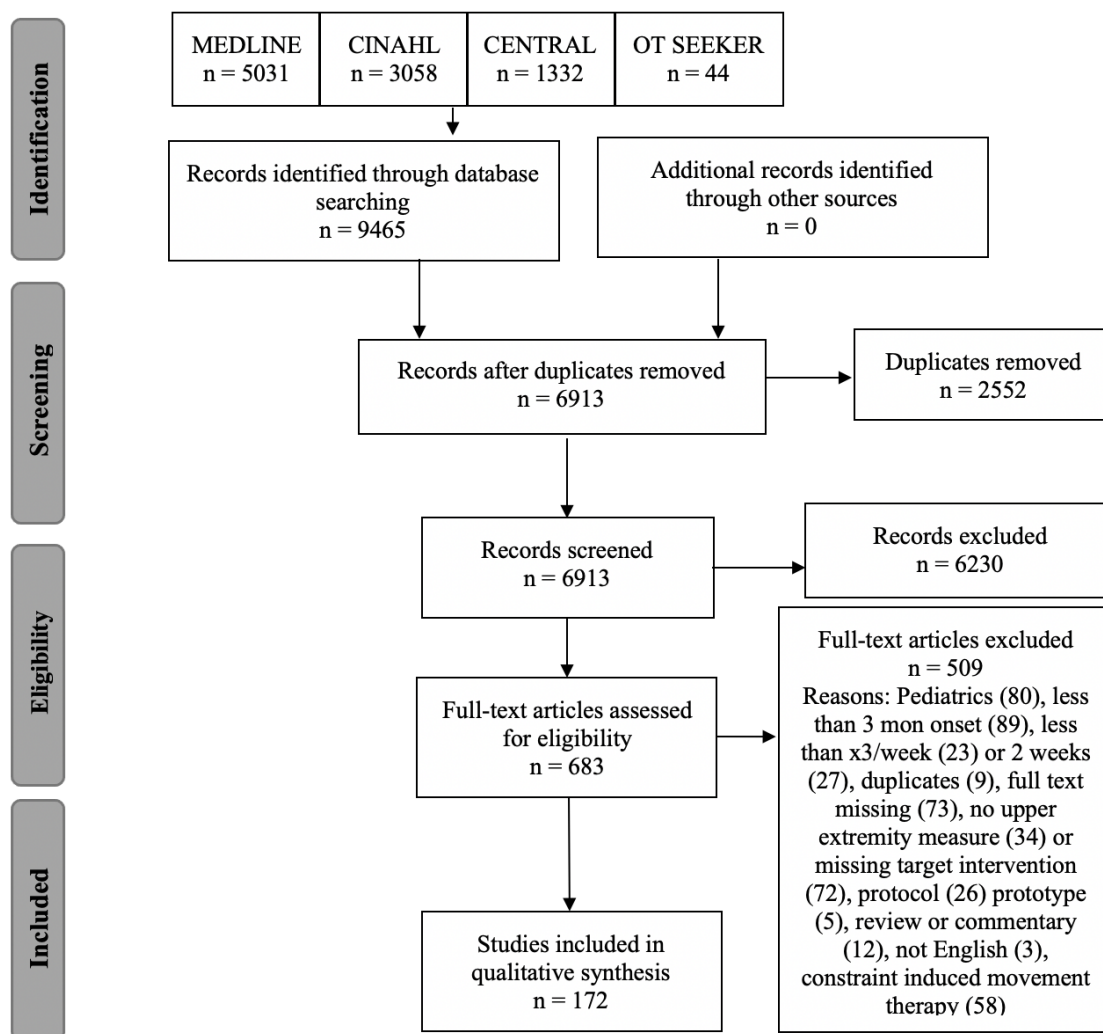
650 **Figure 1. Study Selection PRISMA Flow Diagram for the Scoping Review.** *mon*, months; *n*,

651 number of articles; **PRISMA**, Preferred Reporting Items of Systematic Reviews and Meta-

652 analyses

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