Do people with multiple sclerosis perceive upper limb improvements from robotic-mediated therapy? A mixed methods study

Tedesco Triccas L[a], Maris A[a], Lamers I[a,b], Calcius J[a], Coninx K[c], Spooren A[a], Feys P[a,b]

a REVAL, Faculty of Rehabilitation Sciences, Hasselt University, Diepenbeek, Belgium

b UMSC Hasselt-Pelt (universitair MS centrum), Belgium

c HCI and eHealth, Faculty of Sciences, Hasselt University, Diepenbeek, Belgium

Corresponding Author

Dr Lisa Tedesco Triccas

REVAL, Faculty of Rehabilitation Sciences,

Hasselt University, Diepenbeek,

Belgium

Email: lisa.tedescotriccas@uhasselt.be

Declarations of interest: none

Highlights

- Experiences of rehabilitation technology using mixed methods have been rarely explored in people with multiple sclerosis
- Robot-mediated upper limb therapy resulted in positive experiences on upper limb impairments for people with multiple sclerosis
- Expectations of participants were rather low at baseline but increased with observed functional benefits
- Long-term rehabilitation programs involving rehabilitation technology should be considered for people with multiple sclerosis

Abstract

Background: Robot-mediated training is increasingly considered as a rehabilitation intervention targeting upper limb disability. However, experiences of such an intervention have been rarely explored in the multiple sclerosis population. This mixed methods study sought to explore the impact of an eight week upper limb robotic intervention on experiences of people with multiple sclerosis.

Methods: Eleven participants (Median EDSS- score: 6.5) with moderate to severe upper limb impairment, performed eight week robot- mediated training of the most affected arm. The training involved a virtual learning platform called I-TRAVLE with duration of 30 minutes per training session, twice to three times per week. Two subjective questionnaires with items from the Intrinsic Motivation Inventory (IMI) and Credibility and Expectancy Questionnaire (CEQ) were collected bi-weekly during the intervention. Approximately one month after completing the training, three focus groups were conducted. Main themes were identified using thematic analysis.

Results: Results from the IMI and CEQ indicated high patient satisfaction and expectation that the intervention will be beneficial for them. Two main themes were identified: 1) Effect of the intervention on impairment and activity in that participants felt that there was a positive impact of the training on strength and endurance and during activities of daily living and that is met their expectations; 2) Experiences based on system usage from the system in that participants expressed feelings of motivation and self-improvement. The participants also perceived the training as enjoyable and concluded that the use of games instigated a competitive spirit between the participants.

Conclusions: Robot-mediated training could have a motivating effect and induce a general positive experience while reducing disabilities of people with multiple sclerosis.

Keywords: upper limb dysfunction, rehabilitation health technology, robotic-mediated therapy, experiences, views

1. Introduction

Multiple sclerosis (MS) is a demyelinating central degenerative nervous system disease causing visual, motor, sensory, cognitive, autonomic dysfunctions [1]. One main problem faced by people with MS is upper limb dysfunction, experienced by 66% of the population [2, 3]. Upper limb dysfunctions are usually caused by muscle weakness, sensory impairment and coordination problems [4]. As a result, this has a major impact on their independence during activities of daily living (ADL) [5, 6].

Rehabilitation is usually recommended to ensure that people with MS can preserve and retain their level of function. Research has shown the potential of rehabilitation to enhance upper extremity function and activity [7]. In the last decade, different technologic rehabilitation tools such as virtual reality and robot therapy became more available to improve upper limb dysfunction [8] which can be used as adjacent cost-effective therapy modalities [9]. Such technological tools could provide highly repetitive movements of the upper limb and accurate feedback on performance which is sometimes difficult to achieve through conventional rehabilitation[10, 11]. With the use of technological devices, there are therefore new opportunities to train and improve upper limb function in people with MS [12]. A recent study has identified that robot therapy resulted in increased upper limb function and muscle activity in people with MS [13]. However, there seems to be a lack of strong evidence that robot therapy could be superior on outcome measures of body function and activity level [13, 14]. However, the currently used quantitative clinical measures do not capture all aspects that patients experience from an intervention.

Usage and recognition of the value of qualitative research has been increasing in neurological rehabilitation research [15, 16]. Qualitative methods such as interviews or focus groups allow for in-depth exploration of the experiences and perceptions of patients, and at the same time could create added knowledge to quantitative methods to improve rehabilitation programs. Patients' perception could provide user-centered information on why some rehabilitation programs are successful or on those programs which are not [17]. Views and experiences of upper limb robot therapy have been explored in people with stroke, traumatic brain injury and spinal cord injury [16, 18, 19]. Participants felt that robot therapy was engaging, enjoyable and beneficial for their affected arm. In addition to technological challenges, barriers were also encountered by users such as fatigue or difficulty. This type of research is also relevant for multiple sclerosis, as patients may expect rather deterioration of arm function due to the progressive and chronic condition. Mixed methods [20] involving qualitative in addition to quantitative approaches in studying the (subjective) experience of the upper limb or rehabilitation technology in people with MS are rarely used. Very recently, during interviews, two patients with MS also expressed that an upper limb technology-based system called the i-ACT was an added tool in neurological rehabilitation, an alternative system than usual care and that it instilled feelings of motivation [21].

Prior to the research presented in this paper, first a pilot RCT was conducted involving 17 people with MS comparing the effects of additional robot-supported training to conventional treatment only [14]. Additional training consisted of 3 weekly sessions of 30 min interacting with the HapticMaster (HM) robot within an individualised virtual learning environment (I-TRAVLE). From the pilot RCT, it was found that three dimensional movement tasks during training, were performed in less time. However, no significant changes for any clinical measure were found in both groups, although observational analyses indicated meaningful improvements on the motor impairments in persons with more marked upper limb dysfunction. Second, an interventional study was conducted in people with MS and stroke with an updated virtual learning environment and with a higher dosage of training (20 hours) albeit only partly supervised [12]. In order to obtain an in-depth view on the potential behavioural effects that occurred from the aforementioned study, identification of the subjective experience of participants was therefore important [22]. Therefore, this research embedded in the larger project used quantitative (questionnaires) and qualitative methodologies (focus groups) to address the main research question: ‘how do people with

MS experience the 8-weeks I-TRAVLE training of the upper limb with regard to their functioning and what is their appreciation of the training system'.

2. Materials and methods

2.1 Participants

Participants with upper limb impairment were recruited from the Noorderhart rehabilitation centre in Overpelt, Belgium, using the same inclusion and exclusion criteria reported in Maris et al., (2018). Prior to participation, a written informed consent was obtained.

2.2 Study design and training set-up

The training set-up consisted of eight weeks of high intensity training with the I-TRAVLE system and HM (T0-T4) (Figure 1). The most impaired arm was selected for training. Participants attended five 1-hour training sessions per 2 weeks (2-3x/week) for 8 weeks. The sessions were supervised by a trained therapist with the first 30 minutes involved training sessions followed by 30 minutes break to avoid fatigue. The participants then trained autonomously during the second 30 minutes, while they could choose the exercises and games. The therapist provided feedback on a participant's performance after each training session.

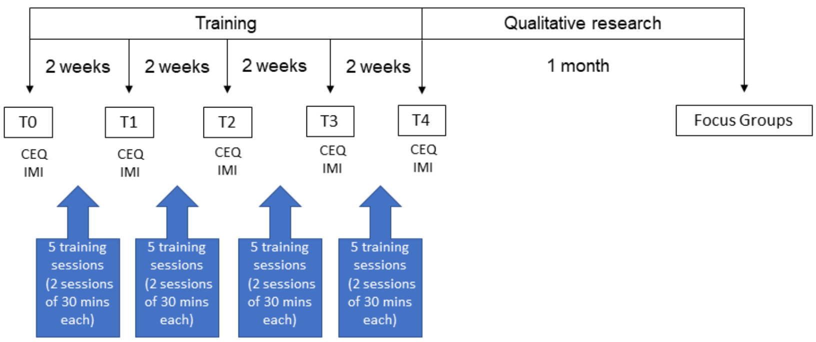

Figure 1. Timeline of the intervention, administraion of the Credibility and Expectancy Questionnaire (CEQ) Intrinsic Motivational Inventory (IMI) and focus group

The HM (MOOG Inc. in Nieuw Vennep, Netherlands) which was designed to train movements of the proximal upper limb (shoulder and elbow). By using the haptic feedback from the HM, the participant in seated position is either supported or challenged during the performance of movements with the arm. By means of an ADL gimbal, participants were able to move the arm around in virtual learning environments shown on the screen.

I-TRAVLE is an acronym for ‘Individualised Technology supported Robot-Assisted Virtual Learning Environment’ developed to train different skill components of arm movement, such as reaching, lifting, transporting, pushing, pulling and rubbing. By means of the serious games several skill components were combined (penguin game, watering the flowers, arkanoid and chicken and egg). The difficulty level was automatically adapted, based on the performance of the participant during the last two training sessions [23]. The intensity was individualized where the haptic feedback, guidance of robot to direct path, workspace, difficulty level of the game (more precision needed, distractors etc) was adapted by the therapist.

2.3 Quantitative research method

A interventional study was conducted in which clinical outcome measures consisted of upper limb active range of motion, handgrip strength, function, manual ability and perceived fatigue and strength. The measures were conducted at baseline, post-intervention and at three months follow-up and results have been reported previously [12].

Here, we report on four items of the Credibility and Expectancy Questionnaire (CEQ) [24] and three subscales of the Intrinsic Motivational Inventory (IMI) [25] that were administered at T0, T1, T2, T3 and T4 (Figure 1). The four items selected from the CEQ were :i) credibility of training; ii) expectation of success of the intervention to improve ADL movements; iii) expectation of success of the intervention to decrease current impairment and iv) confidence to advise this type of intervention to others. Items from the CEQ are scored from one till nine: one refers to no agreement and nine refers to high agreement. The three subscales from the IMI were selected based on identifying the experiences of the patients and these were: v) credibility of intervention; vi) enjoyment of the intervention and vii) satisfaction of achievements during intervention. These items were scored from one till seven: one identifies disagreement and seven identified total agreement.

2.4 Qualitative research method

In order to generate an in-depth understanding of the experiences of the intervention by people with multiple sclerosis, focus groups were performed. This involves a researcher gathers a group of individuals to discuss a specific topic with the aim of obtaining complex personal experiences and attitudes [26-28]. A focus group was preferred in favor of in-depth interviews because we wanted to understand how the purposely selected individuals interacted in a group and expressed their feelings. Focus groups were organised one month after the end of the training, in the Noorderhart Rehabilitation centre, Overpelt. The audio recording device was placed at the centre of the table and all participants were made aware of this. Each focus group lasted approximately an hour. An independent moderator conducted the two first focus groups using a predefined topic list. For the third focus group started, another moderator was appointed who had however attended the previous two sessions and was trained by the initial moderator. Additionally, two independent researchers were present to observe non-verbal communication and behaviour during all the focus groups.

2.5 Quantitative and qualitative data analysis

Descriptive analysis using mean scores was conducted to analyse the date of the first four items from the subjective experience questionnaire. Mean scores of the items from the CEQ and IMI from the subjective experience questionnaire were analysed and evaluated by the Wilcoxon signed ranks test using the statistical program R. The p value of <0.05 was set to assess for significant differences over time at time-points

In order to analyse the open questions asked in the focus groups, the following steps were conducted by two researchers (1) the audio recordings were transcribed verbatim; (2) data that compromised participants' anonymity or identified specific healthcare services were deleted from the transcripts; (3) familiarisation of the data by reading and rereading the transcriptions attentively and highlighting sections keeping the research question in mind; (4) generating initial codes, identifying and reviewing key themes using thematic analysis [29]; (5) findings were then cross-referenced and (6) naming the final themes and selecting appropriate quotes to support each theme. Triangulation, involving merged data integration for accordance and discordance between quantitative and qualitative results, was then carried out [30].

3. Results

Eleven participants with MS (median age 54 years and Median EDSS- score was 6.5) completed the questionnaire items and took part in the focus groups. Four participants took part in the first focus group, five in the second focus group and two in the last focus group. Six participants had secondary progressive MS, three participants had relapsing progressive MS and lastly two participants were diagnosed with primary progressive MS.

3.1 Quantitative Results from interventional study and questionnaire

As reported elsewhere, the training resulted in significant improvements in active shoulder ROM, handgrip strength, perceived upper limb strength and activities [12].

The high median scores of 7 or 8 on the CEQ items indicated that the participants accounted the intervention with high credibility (Table 1). During the intervention, participants remained confident that this type of intervention is successful in diminishing their upper limb limitations. There was an advice to others to also engage in I-TRAVLE training which was not altered significantly over time (p=0.652). During the eight weeks of intervention, the median scores of the IMI remained relatively stable and high. This indicates that participants were satisfied and enjoyed the intervention after eight weeks.

Table 1: **CEQ and IMI of the subjective experience questionnaire (N=11)**

CEQ (0-9)		T1		T2		T3		T4		p-value
	Credibility	7	[7-9]	7	[6-7]	7	[7-8]	7	[7-8]	0.159
	Success ADL	7	[6-7]	7	[5-7]	6	[5-7]	7	[6.75-9]	0.4093
	Success limitations	7	[6-7]	7	[6-8]	7	[5-7]	7	[5-7.25]	0.9906
	Advise	8	[7-9]	8	[7-9]	7	[7-8]	6.75	[6.75-9]	0.652
IMI (0-7)										
	Valuable	7	[6-7]	7	[6-7]	6	[5-7]	5	[5-7]	0.0909
	Fun experience	7	[7-7]	7	[6-7]	7	[6-7]	6.75	[6.75-7]	0.3357
	Satisfaction	6	[5-7]	6	[5-7]	7	[6-7]	6	[6-7]	0.2276

Values are median and [interquartile range]. Significance level of Friedman test set at $p<0.05$

IMI: Intrinsic motivation index; CEQ: Credibility and expectancy questionnaire

3.3 Qualitative results from focus groups

Two main themes were identified from the thematic analysis: (i) user experiences with the system and (ii) effect of impairment and activity. Quotes supporting each theme are presented in Table 2.

Theme 1: Effect of robot therapy on impairment and activity

It appeared that, regarding the participants' upper limb use, progression was made, especially in relation to impairment such as endurance, strength and mobility when using their upper limb. Due to the improved endurance participants were able to use their weak arm for a longer period of time and they also reported an accelerated recovery of their level of fatigue. Also, whereas at first the arm was rather stiff and it was difficult to lift, after the training, the participants had a more flexible feeling in their arm and it was much easier to move. Often comparisons were made with feelings of extra weight on their arm.

Looking at the mobility of the arm, other aspects such as improved ability to perform fine movements and a better quality of movement were stated. In the beginning of the intervention, participants felt that there was little to no mobility in their upper limb. However after the training finished, one of the participants stated that he could effortlessly move his arm with a target position in mind. It also became obvious that although positive changes in their upper limb were present, it was still difficult for participants to describe their feelings.

As training continued, more and more improvements were noticed. The importance of continuation of training at the end of the intervention, was also noted, since the participants felt their upper limb function was deteriorating. While a majority of the participants felt that they became stronger in their arm related to changes in mobility, endurance and strength, they seemed to be more motivated when changes were felt in specific activities and in participation.

Table 2: Themes with the supported quotes from the participants

Theme	Supported quotes in Dutch and English
Effect of robot therapy on impairment and activity	*Een standbeeld, mijn arm aan de linkerkant is altijd een standbeeld…Soms krijg ik die gewoon echt niet in gang.” A statue, my arm on the left is always a statue...sometimes I just can't get it going* *“vooral in kracht en uithouding, een verbetering toch wel” “especially in strength and endurance, an improvement surely”*
	“vroeger moest ik altijd die arm helpen om die op tafel te krijgen en nu gaat dat vanzelf” “I used to always have to help that arm to get it on the table and now it goes without saying”
	“Ja, ik heb dat met mijn keyboard, ik voel dat ook aan, mijn arm was sneller moe en nu kan ik langer spelen.” “*Yes, I have that with my keyboard, I can feel it too, my arm was tired faster and now I can play longer.”*
	“Ik kan niet zeggen dat het spectaculair verbeterd is, maar het zal ook niet slechter zijn geworden.” “I can't say it's improved spectacularly, but it won't have gotten worse either.”
User experiences with the system	*“Maar ge geraakt het wel gewoon ook wel. Bijvoorbeeld een pot steekt ge tussen uw benen en draait ge die met rechts open eh. Ja, ge leert zonder linkse hand ook een beetje werken eh.”* “*but you just get it. For example, you put a pot between your legs and open it with your right eh. Yes, you also learn to work a little without a left hand, eh.*

Participants reported being able to eat better and being more efficient in using the mouse of the computer. One participant explained that it was now possible to carry her grandchild again, while another stated that it was easier to open jars. More so, most of the participants felt that they improved most on the endurance level mainly related to household chores, like being able to peel more potatoes and with better stability, holding the handle of a pan during cooking, or being able vacuum for a longer period. But aside from these improvements, even progress was made so that participants could once again enjoy their hobbies, like playing the keyboard.

All these improvements also led to better bimanual skills. It was easier for participants to prepare their sandwiches or using both knife and fork again while eating. Lastly there were also some minor improvements for some participants on the participation level. These improvements were being able to hug their loved ones or being able to carry their grandchildren again. The participants also tended to do more things with their friends now that they improved their arm skills, such as going to a restaurant.

While most of the participants only reported positive benefits from the robot-mediated training, one of the participants explained that he felt little to no changes after the training was completed.

Theme 2: **User experiences with the system**

When the participants where asked how they experienced the training sessions, feedback was overwhelmingly positive. The aspect of gaming instilled feelings of competitiveness, which in turn led to participants enjoying the training sessions. The intensity of the intervention was felt for most of the participants as good and constant, but rather difficult for some of them, to the extent that they were pushed to their limits. This difficulty was described by the participants as if their endurance in the second half hour of training had diminished. When asked if this type of training met their expectations, the participants were very affirmative. In most cases, they participated without much hope or expectations. As training continued, more and more improvements were noticed. This immediately correlates to the hope of participants to have the opportunity to access this type of training in the future. Finally, one negative impact after the training finished was that they felt that the improvements they had obtained during the intervention were slowly deteriorating and found creative ways to using their upper limb, one month after the intervention. Furthermore, one participant expressed that she or he enjoyed being at the training centre. It was a practical manner to pass time and meet people. The participant could often enjoy the company of other participants and liked to have a chat with them. This was apparently a nice way to enjoy the day, rather than being at home. Lastly, another example was the fact that their mere participation motivated them to help other people with MS with upper limb impairments, by providing researchers more knowledge about the using different interventions to aim at improving disability in people with MS.

3.4 Triangulation of data

Overall, there were no instances of dissonance between any of the quantitative and qualitative data. Improvement in factors relating to body structure and function such as upper limb muscle strength were in agreement between the quantitative and qualitative data. The qualitative data gave more in-depth insights into this finding that having improvement in ADL, in addition with participation instilled more motivation than improvement in body structure and function. There was also agreement in feelings of satisfaction and enjoying the intervention.

4. Discussion

The presented research reports on the explored experiences of robot-mediated therapy for the upper limb of people with MS using both quantitative and qualitative methods. In summary, the results showed that participants enjoyed the intervention and the intervention improved their arm and hand impairment such as smoothness of movement, strength and use of arm. Moreover, they felt that the intensity was at the right level but also felt fatigued in the second part of the session. Qualitative data analysis also showed that participants wanted to continue the robot-mediated therapy since they were afraid that they would lose all of the beneficial effects of the intervention on their upper limb.

Overall using a mixed methodology to understand the experiences of robot mediated therapy was beneficial to gain in-depth information about the feasibility of such an intervention. This type of methodology is increasingly applied to explore experiences of various factors such as understanding the impact of fatigue or needs of mHealth in the MS field [31-33]. Overall, participants were positive about the robot-mediated therapy program. As found in other neurodisabling conditions, positive experiences of robot therapy on upper limb impairment and function were expressed [16, 34]. Although a virtual learning environment was incorporated in the setup used in this study, the HM's software did not incorporate wrist and hand movements. However, even without that functionality in the application, improvement in wrist and hand function was perceived by the participants. This is contradictory to similar robotic studies involving people with stroke where changes in hand function such as ability to use the keyboard again was not experienced by participants [16, 34]. Therefore, it is rather surprising that the participants with MS felt the opposite, which could be probably due to more confidence in using their upper limb in daily life. Recently, a virtual reality program associated with serious games incorporating hand movements has been found beneficial at impairment level in thirty people with MS [35]. Therefore, incorporating virtual reality platforms combined with other technologies that focus on both the arm and hand could have a superior effect [36].

People with MS are usually motivated to take part in rehabilitation programs to increase self-efficacy and decrease their symptoms [37]. Using multiple innovative technologies in the rehabilitation process of people with MS increases their commitment and motivation and may lead to an improvement of their quality of life [38]. Participants often started the intervention without expectations, but with the hope that they would improve their arm function. Although we cannot state that a robot-mediated intervention is superior to traditional rehabilitation, we can assume that it has advantages in improvement in the velocity, linearity and smoothness of movements as well as on functionality of the upper limb [39, 40]. Also the fact that the intensity is adjusted by the level of haptic feedback resulted in participants being even more motivated. In contrary to stroke participants, a fine line between the intensity and motivation of participants was observed. If the intensity was too high without support and it became difficult to perform the various tasks, then the motivation would decrease leading to a participant into a vicious circle of frustration due to the high intensity of the exercises [41].

After the robot therapy program, not only participants felt that there were improvements in their arm function but also their subjective experiences were modified. As identified in similar research [21], participants felt more motivated when an intervention addressed their impairments, activity limitations and also their participation. This could be due to the participants experiencing moderate to severe impairments. This category of people with MS are more likely to have restrictions in participation in domestic and outdoor activities [42]. The importance of integrating rehabilitation technology in clinical and community settings is sometimes forgotten for people with MS and their caregivers which could eventually have an impact on their participation and quality of life.

The present study documented the qualitative experiences of persons participating in technology-supported rehabilitation. The patient experiences are valued, and can contribute to shape future intervention delivery methods, and ingredients of a larger RCT. A major strength of this paper is employing a user-centred approach by using mixed methods in exploring the experiences of people with MS of robot-mediated therapy. Through this approach we took into account an individual's perceptions of the system behind physical and psychosocial activities which could differ from expectations of professionals working in health sciences and also engineering [43]. As a qualitative perspective, the use of focus groups was feasible allowing group interaction, discussion and easier to gather data in a short amount of time. However, the change of moderator in the third focus group was not favourable. Also the fact that the third focus group had only two participants could be considered as a limitation of the research. The CQE and IMI have shown significant results however, these results need to be interpreted with caution since the sample size was small.

5. Conclusion

From this mixed-methods study it could be concluded that robot-mediated intervention results in positive effects on subjective experiences on upper limb impairments, and on activity limitation and participation from the qualitative data. It results in feelings of content and motivation from the system. From the research it was concluded that participants wanted a long-term rehabilitation program involving robot-mediated therapy. Addressing how this could be implemented in clinical practice is essential.

6. Acknowledgments

The authors would like to thank the Rehabilitation Centre Blixembosch for their cooperation regarding the development of the I-TRAVLE system (2009–2012), master students and participants that took part in the research.

This work was supported by Interreg (INTERREG IVA-VLANED-1.58: “I-TRAVLE” project).

References

1. Noseworthy, J.H., et al., *Multiple sclerosis.* N Engl J Med, 2000. **343**(13): p. 938-52.
2. Spooren, A.I., A.A. Timmermans, and H.A. Seelen, *Motor training programs of arm and hand in patients with MS according to different levels of the ICF: a systematic review.* BMC neurology, 2012. **12**(1): p. 1-11.
3. Bertoni, R., et al., *Unilateral and bilateral upper limb dysfunction at body functions, activity and participation levels in people with multiple sclerosis.* Multiple Sclerosis Journal, 2015. **21**(12): p. 1566-1574.
4. Lamers, I., et al., *Associations of upper limb disability measures on different levels of the International Classification of Functioning, Disability and Health in people with multiple sclerosis.* Phys Ther, 2015. **95**(1): p. 65-75.
5. Spooren, A.I., A.A. Timmermans, and H.A. Seelen, *Motor training programs of arm and hand in patients with MS according to different levels of the ICF: a systematic review.* BMC Neurol, 2012. **12**: p. 49.
6. Yozbatıran, N., et al., *Motor assessment of upper extremity function and its relation with fatigue, cognitive function and quality of life in multiple sclerosis patients.* Journal of the neurological sciences, 2006. **246**(1-2): p. 117-122.
7. Lamers, I., et al., *Upper limb rehabilitation in people with multiple sclerosis: a systematic review.* Neurorehabilitation and neural repair, 2016. **30**(8): p. 773-793.
8. Bastiaens, H., et al., *Facilitating robot-assisted training in MS patients with arm paresis: a procedure to individually determine gravity compensation.* IEEE Int Conf Rehabil Robot, 2011. **2011**: p. 5975507.
9. Gijbels, D., et al., *The Armeo Spring as training tool to improve upper limb functionality in multiple sclerosis: a pilot study.* J Neuroeng Rehabil, 2011. **8**: p. 5.
10. Merians, A.S., et al., *Virtual reality–augmented rehabilitation for patients following stroke.* Physical therapy, 2002. **82**(9): p. 898-915.
11. Maggio, M.G., et al., *Virtual reality in multiple sclerosis rehabilitation: A review on cognitive and motor outcomes.* Journal of clinical neuroscience, 2019. **65**: p. 106-111.
12. Maris, A., et al., *The impact of robot-mediated adaptive I-TRAVLE training on impaired upper limb function in chronic stroke and multiple sclerosis.* Disability and Rehabilitation: Assistive Technology, 2018. **13**(1): p. 1-9.
13. Gandolfi, M., et al., *Effects of high-intensity robot-assisted hand training on upper limb recovery and muscle activity in individuals with multiple sclerosis: a randomized, controlled, single-blinded trial.* Frontiers in neurology, 2018. **9**:905.
14. Feys, P., et al., *Robot-supported upper limb training in a virtual learning environment: a pilot randomized controlled trial in persons with MS.* Journal of neuroengineering and rehabilitation, 2015. **12**(1): p. 1-12.
15. Kuper, A., S. Reeves, and W. Levinson, *An introduction to reading and appraising qualitative research.* BMJ, 2008. **337**: p. a288.
16. Tedesco Triccas, L., et al., *A qualitative study exploring views and experiences of people with stroke undergoing transcranial direct current stimulation and upper limb robot therapy.* Topics in sTroke rehabiliTaTion, 2018. **25**(7): p. 480-488.
17. Barker, R.N. and S.G. Brauer, *Upper limb recovery after stroke: the stroke survivors' perspective.* Disabil Rehabil, 2005. **27**(20): p. 1213-23.
18. Louie, D.R., et al., *Patients' and therapists' experience and perception of exoskeleton-based physiotherapy during subacute stroke rehabilitation: a qualitative analysis.* Disability and Rehabilitation, 2021: p. 1-9.
19. Laparidou, D., et al., *Patient, carer, and staff perceptions of robotics in motor rehabilitation: a systematic review and qualitative meta-synthesis.* Journal of neuroengineering and rehabilitation, 2021. **18**(1): p. 1-24.
20. Creswell, J.W. and M. Hirose, *Mixed methods and survey research in family medicine and community health.* Family Medicine and Community Health, 2019. **7**(2).
21. Knippenberg, E., et al., *Motivation, usability, and credibility of an intelligent activity-based client-centred training system to improve functional performance in*

neurological rehabilitation: an exploratory cohort study. International Journal of Environmental Research and Public Health, 2021. **18**(14): p. 7641.
22. Calsius, J., et al., *"How to conquer a mountain with multiple sclerosis". How a climbing expedition to Machu Picchu affects the way people with multiple sclerosis experience their body and identity: a phenomenological analysis.* Disabil Rehabil, 2015: p. 1-7.
23. Octavia, J.R. and K. Coninx, *Adaptive personalized training games for individual and collaborative rehabilitation of people with multiple sclerosis.* BioMed research international, 2014. **2014**.
24. Devilly, G.J. and T.D. Borkovec, *Psychometric properties of the credibility/expectancy questionnaire.* Journal of behavior therapy and experimental psychiatry, 2000. **31**(2): p. 73-86.
25. McAuley, E., T. Duncan, and V.V. Tammen, *Psychometric properties of the Intrinsic Motivation Inventory in a competitive sport setting: A confirmatory factor analysis.* Research quarterly for exercise and sport, 1989. **60**(1): p. 48-58.
26. Kitzinger, J., *The methodology of focus groups: the importance of interaction between research participants.* Sociology of health & illness, 1994. **16**(1): p. 103-121.
27. Morgan, D.L., *Focus groups.* Annual review of sociology, 1996. **22**(1): p. 129-152.
28. O. Nyumba, T., et al., *The use of focus group discussion methodology: Insights from two decades of application in conservation.* Methods in Ecology and evolution, 2018. **9**(1): p. 20-32.
29. Gavin, H., *Thematic analysis.* Understanding research methods and statistics in psychology, 2008: p. 273-282.
30. Curry, L. and M. Nunez-Smith, *Assessing quality in mixed methods studies.* Mixed Methods in Health Sciences Research: A Practical Primer, New Haven: SAGE Publications, Inc, 2015: p. 169-200.
31. Giunti, G., et al., *Exploring the specific needs of persons with multiple sclerosis for mHealth solutions for physical activity: mixed-methods study.* JMIR mHealth and uHealth, 2018. **6**(2): p. e37.
32. Penner, I.-K., et al., *Exploring the impact of fatigue in progressive multiple sclerosis: a mixed-methods analysis.* Multiple Sclerosis and Related Disorders, 2020. **43**: p. 102207.
33. Simacek, K.F., et al., *The impact of disease-modifying therapy access barriers on people with multiple sclerosis: mixed-methods study.* Journal of medical Internet research, 2018. **20**(10): p. e11168.
34. Meadmore, K.L., et al., *Functional electrical stimulation mediated by iterative learning control and 3D robotics reduces motor impairment in chronic stroke.* Journal of neuroengineering and rehabilitation, 2012. **9**(1): p. 1-11.
35. Cuesta-Gómez, A., et al., *Effects of virtual reality associated with serious games for upper limb rehabilitation inpatients with multiple sclerosis: randomized controlled trial.* Journal of NeuroEngineering and Rehabilitation, 2020. **17**(1): p. 1-10.
36. Massetti, T., et al., *Virtual reality in multiple sclerosis–a systematic review.* Multiple sclerosis and related disorders, 2016. **8**: p. 107-112.
37. S., K., *Exercising with multiple sclerosis- insights into meaning and motivation.* Adapt Phys Activ Q, 2009: p. 16.
38. Manuli, A., et al., *Patients' perspective and usability of innovation technology in a new rehabilitation pathway: An exploratory study in patients with multiple sclerosis.* Multiple sclerosis and related disorders, 2020. **44**: p. 102312.
39. Carpinella, I., et al., *Robot Training of Upper Limb in Multiple Sclerosis: Comparing Protocols With or WithoutManipulative Task Components.* Ieee Transactions on Neural Systems and Rehabilitation Engineering, 2012. **20**(3): p. 351-360.
40. Carpinella, I., et al., *Robot-based rehabilitation of the upper limbs in multiple sclerosis: feasibility and preliminary results.* J Rehabil Med, 2009. **41**(12): p. 966-70.

41. Sabini, R.C., M.P. Dijkers, and P. Raghavan, *Stroke survivors talk while doing: development of a therapeutic framework for continued rehabilitation of hand function post stroke.* J Hand Ther, 2013. **26**(2): p. 124-30; quiz 131.
42. Conradsson, D., et al., *Activity limitations and participation restrictions in people with multiple sclerosis: a detailed 10-year perspective.* Disability and rehabilitation, 2019: p. 1-8.
43. Tedesco Triccas, L., et al., *A nation-wide survey exploring the views of current and future use of functional electrical stimulation in spinal cord injury.* Disability and Rehabilitation: Assistive Technology, 2021: p. 1-11.