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Feasibility and usability of a new home-based immersive virtual reality headset-based dexterity training in multiple sclerosis

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ABSTRACT

Background: Impaired manual dexterity is frequent and disabling in patients with multiple sclerosis (MS), affecting activities of daily living and quality of life.
Objective: The aim of this study was to evaluate the feasibility, usability and patient engagement/satisfaction of a home-based immersive virtual reality (VR) headset-based dexterity training in persons with multiple sclerosis (pwMS). In addition, preliminary efficacy data on the impact of this new training on manual dexterity were collected.
Methods: Single arm prospective study. After a waiting period of two weeks, pwMS performed a specifically developed home-based VR headset-based dexterity training using the Oculus quest 2 for two weeks with five training sessions/week, each session for approximately 20 minutes. Primary endpoints were feasibility (measured by the adherence rate), usability (System Usability Scale, SUS) and patient engagement/satisfaction (Custom User Engagement Questionnaire, CUEQ). Secondary exploratory efficacy endpoints, measured before and after the waiting period as well as after the training intervention, were the Nine-hole-Peg-Test (9HPT), Coin rotation task (CRT), Handheld JAMAR dynamometer, Arm Function in Multiple Sclerosis Questionnaire (AMSQ) and the Multiple Sclerosis Impact Scale 29 (MSIS 29).
Results: Eleven pwMS (mean age 49 ± 10.87 SD, mean EDSS 4.28 ± 1.48 SD) participated in the study. Feasibility (adherence rate: 81.8%), usability (median SUS score 94 (IQR = 78-96)) and patient engagement/satisfaction (median 8 on scale of 1-10) of the VR training was very high. In addition, the CRT for the dominant hand improved significantly after training ($p = 0.03$).
Conclusions: The good results on feasibility, usability, and patient engagement/satisfaction qualify this home-based immersive VR headset-based dexterity training approach for the use in home-based neurorehabilitation in pwMS. Improved fine motor skills for the dominant hand suggest preliminary efficacy, but this needs to be proven in a future randomized-controlled trials.

1. Introduction

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system and the most common cause of non-traumatic disability in young adults in western countries (Kamm et al., 2014). Despite increasing therapeutic options to ameliorate the disease course, most patients suffer from persistent neurological deficits over time. Impaired manual dexterity is frequent, affecting approximately three-quarters of persons with MS (pwMS) (Johansson et al., 2007) (Chruzander et al., 2013). It is a relevant handicap that independently impairs activities of daily (ADL) living and quality of life (QoL) and is associated with loss of work and the need providing care (Chruzander et al., 2013) (Yozbatiran et al., 2006). Impaired manual dexterity occurs early, however is preserved longer in the disease course compared to walking capabilities leading to a different meaningfulness of manual dexterity throughout disease progression (Johansson et al., 2007) (Giovannoni et al., 2017). In early stages of the disease, arm-hand function is important, for example, for activities such as driving a car

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or doing creative activities. In later stages with usually lower extremity functions worsening first, upper extremity function is important to maintain daily functions such as dressing and eating, using a wheelchair, performing intermittent catheterization, or using a computer (Giovannoni et al., 2017) (Thompson et al., 2016). Therefore, manual dexterity is an important symptom for neurorehabilitation to improve ADL and QoL in pwMS (Yozbatiran et al., 2006).

Manual dexterity is usually trained with physical- or occupational therapy in a low-frequency outpatient setting using traditional methods such as "hands-on techniques" (Řasová et al., 2020). In a European survey in MS, accessibility to physical therapy was poor with access to outpatient therapy varying from 34% to 41.3% and inpatient therapy varying from 17.4% to 28.5% (Kobelt et al., 2017). Furthermore, accessibility differed significantly amongst regions and overall frequency of use was low (32.7%) (Kobelt, 2017; Řasová, 2020). With recent technological innovations such as the development of applications (apps) for mobile phones and tablets as well as Virtual Reality (VR) Headsets, new treatment options arise that can be used on their own or as a supplement to classical therapies. Compared to traditional methods such as physical- or occupational therapy, or complex and expensive technological approaches requiring inpatient treatments (Webster et al., 2021), mobile phones, tablets or VR headsets, often already owned by pwMS, can be used as training device independently at home enabling high-frequency home-based training while being efficacious and cost-effective (Yeroushalmi et al., 2022). Patients can be treated who otherwise have no access to therapies due to limited mobility, lack of therapy in the region, travel costs, or lack of time which are main reasons not to participate in classical therapies (Řasová et al., 2020).

In this regard we already performed home-based research projects with conventional training methods and Tablet App Based Dexterity Trainings in MS (Kamm et al., 2015; van Beek et al., 2019a; van Beek et al., 2020; van Beek et al., 2022). However, training with VR Headsets offers additional promising training options and initial trials were already performed (Bertoni et al., 2022).

VR is a computer-generated environment with scenes and objects that appear to be real, making the user feel they are immersed in their surroundings. VR headset devices are one of the technologies with the highest projected potential for growth and likely to become an integral part of our private and professional life (Garrett et al., 2018) (https://www.meta.com). For these reasons, immersive VR devices will probably be highly suitable to be used as medical devices in the future including virtual rehabilitation (Garrett et al., 2018; Yeroushalmi et al., 2022).

Advantages of VR are to create realistic risk-free environments that are not realizable and/or financeable in the real world. These VR environments are easily adaptable to the needs of the user, and the possibility of gamification increases patient motivation (Doumas et al., 2021). As further advantage, VR can be performed in the patient's home and monitored at a distance (telerehabilitation). The home-based setting allows frequent training independently of available hospital or community-based rehabilitation programs which makes training interventions available to a larger group of patients (Yeroushalmi S et al. 2022). In addition, VR devices can be potentially used to measure outcome parameters such as adherence or the efficacy of interventions (Craig et al., 2022; Jost, 2021).

Regarding dexterity training interventions, hand- and finger tracking technologies additionally enable more effective and precise interaction in a natural fashion and an increased immersion and presence, i.e. the subjective experience of being in a highly-immersive virtual environment (Buckingham, 2021).

The aim of this pilot study was therefore to investigate the feasibility, usability and patient engagement/satisfaction of a self-developed home-based immersive dexterity training using a VR Headset (Oculus quest 2) in pwMS. In addition, preliminary efficacy data on the impact of the training program on manual dexterity were collected.

2. Materials and Methods

2.1. Participants

Participants were recruited consecutively through the corresponding author during regular visits at the MS center of the Luzerner Kantonsspital, Switzerland. Patients with relapsing-remitting MS, secondary-progressive MS, or primary-progressive MS according to the 2017 McDonald's criteria, age between 18-75 years were eligible (Thompson et al., 2018). Main exclusion criteria were relapses and/or steroid treatment within the preceding 60 days, rapidly progressive MS and additional diseases or conditions apart from MS that affect manual dexterity or compromise the adequate performance of the study procedures. Each participant provided written informed consent prior to study entry. The study was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki, 2023) and approved by the Ethics Committee Northwest/Central Switzerland EKNZ (BASEC-Nr. 2022-00032).

2.2. Study design

This was a single-center, single-arm observational study. At screening/baseline (Visit 1), demographic data and efficacy measures (= secondary outcome measures) were collected followed by a 2-weeks waiting period. Afterwards efficacy measures were repeated, and pwMS were instructed into the home-based training intervention by the corresponding author (Visit 2). After the 2-weeks training period, efficacy measures were repeated, and feasibility and usability outcome measurements (= primary endpoints) were performed (End of study Visit 3) (Fig. 1).

2.3. Study procedures

At screening/baseline, demographic data (age, gender), handedness, disease duration, date of MS diagnosis, MS type, current medication and diseases relevant to the study as well as experience with VR devices (yes/no) were collected. The Expanded Disability Status Scale (EDSS) score was taken from the last routine appointment (Kurtzke et al., 1983) and the Single Digit Modality Test (SDMT) was performed as cognitive screening test (Benedict et al., 2017).

Primary outcome measures. The primary endpoints were feasibility, usability and patient satisfaction. Feasibility was measured by the adherence to the protocol, usability by the System Usability Scale (SUS) and patient satisfaction by a Custom User Engagement Questionnaire (CUEQ).

Based on our previously published pilot study (van Beek, 2019b) (van Beek, 2020), feasibility was measured with the adherence rate being the ratio of the number of sessions performed (SP) and the prescribed number of sessions (PS), which is 10, so ((SP/PS) * 100%) = ((SP/10) * 100%). An adherence rate of $\geq$80% was considered as good (Vanbellingen et al., 2017). SP were extracted from the Oculus quest 2. Each time the training intervention is started is stored on the device inside a SQL lite database (SQLite file). The date and time used are based on the OS of the headset. The data is stored continuously as the application is used. In the first iteration, the data can only be accessed directly on the headset and can be downloaded through adb (developer tool for android).

Regarding the usability of the system, the SUS was performed after completing the intervention (Visit 3). The SUS is a well-validated questionnaire, consisting of a 10-item Likert scale. Each item was scored from 0 ("strongly disagree") to 4 ("strongly agree") which takes three usability criteria into account: effectiveness, efficiency, and satisfaction. The total score is obtained by multiplying the mean sum value by 2.5. The SUS score has a range of 0% to 100% with higher values indicating better usability. A score of 70% to 100% represents acceptable to excellent usability (Brooke et al., 1986, Borsci et al.,

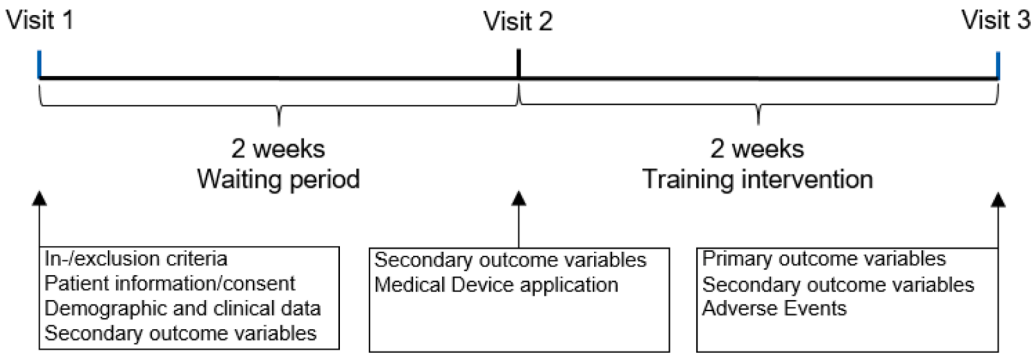

Fig. 1. Study design. Single-center, single-arm observational study. After a 2-weeks waiting period (Visit 1 – Visit 2), participants started the home-based training intervention (Visit 2). After the 2-weeks training intervention, efficacy measures (= secondary endpoints) were repeated, feasibility and usability outcome measurements (= primary endpoints) were performed, end the study ended (Visit 3).

2009).

A Custom User Engagement Questionnaire (CUEQ), which was previously developed by us and applied in prior feasibility trials, was used to evaluate the training intervention regarding user engagement and satisfaction of the training intervention more specifically (van Beek et al., 2020). The CUEQ was developed based on expert agreement and showed high face and content validity (van Beek et al., 2020). The CUEQ contains two parts. Firstly, seven specific questions related to the content of the VR-based training intervention are scored on a scale ranging from 1 ("bad") to 5 ("excellent") (ie, Q1 = Were the exercises fun to play?; Q2 = Have you improved your fine motor skills?; Q3 = Was it easy to integrate the exercises into daily life?; Q4 = Were the explanations for the execution of each exercise sufficient?; Q5 = Would you recommend this application?; Q6 = Can you take the VR headset easily on the go?; and Q7 = Do you notice improvements in everyday life regarding fine motor skills?). Secondly, participants gave an overall rating of satisfaction with the training intervention ranging from 1 ("very poor quality") to 10 ("excellent quality").

In addition, participants could give further written feedback regarding the training intervention including engagement and satisfaction and were asked to suggest improvements.

Secondary outcome measures. Secondary endpoints were performed every visit to get preliminary and exploratory data on the efficacy of the training intervention on manual dexterity (Fig. 1).

The **Nine Hole Peg Test (9HPT)** is reliable (ICC values 0.80–0.99), valid and sensitive in detecting impaired dexterity in pwMS (Oxford Grice et al., 2003, Yancosek et al., 2009). The time to complete the task was recorded twice on both hands and mean values were taken for each hand. If patients could not perform the 9HPT, an arbitrarily chosen value of 300 seconds was taken.

The **Coin Rotation Task (CRT)** is reliable and valid in assessing manual dexterity in pwMS (Heldner et al., 2014). The time to perform 20 half turns was measured twice on both hands and mean values were taken for each hand. If patients could not perform the CRT, an arbitrarily chosen value of 300 seconds was taken.

The **handheld JAMAR dynamometer** is a reliable (ICC values 0.85 – 0.98) and valid test to measure isometric grip strength of the hands in healthy subjects and in pwMS (Peolsson et al., 2001). It is performed in an upright seating position with 90° flexion of the elbow next to the body. The highest value (kilograms force) of two maximum voluntary grip strength movements was taken for each hand.

The **"Arm Function in Multiple Sclerosis Questionnaire" (AMSQ)** is a patient recorded outcome measure (PROM) evaluating the impact of manual dexterity on ADL in pwMS. The AMSQ was validated in several languages showing good validity, test-retest reliability and inter-observer reliability (Kalkers et al., 2021, Steinheimer et al., 2018).

The **Multiple Sclerosis Impact Scale (MSIS-29)** is valid and reliable in measuring the overall impact of MS on ADL. It contains 29 items comprising to a physical (MSIS-29 physical) and psychological impact scale (MSIS-29 psychological). All items are scored from 'not at all' to 'extremely' on a five-point Likert scale (McGuigan and Hutchinson, 2004).

As safety endpoints, adverse events and dropouts were collected at visits 2 and 3.

Training intervention: The VR headset-based training intervention was specifically developed for this project by the corresponding author in collaboration with the Start-ups "12 Parsec" (Oberfeld 3, 6037 Root, Switzerland), "Holonautic AG" (Felmis-Allee 11, 6048 Horw, Switzerland) and "Westhive" (Hardturmstrasse 161, 8005 Zürich, Switzerland). The commercially available Oculus quest 2 (Meta) was used as VR-Device (Fig. 2). It is a standalone "all in one" immersive VR headset delivered with two hand-held controllers and an embedded hand- and finger tracking technology (https://www.meta.com). The detailed description of the training intervention and its development regarding medical and technical aspects will be publish separately (Kamm et al., in preparation). The training intervention derived from previous successful home-based training interventions with conventional training methods and Tablet App Based Dexterity Trainings in MS in which trainings were performed five days/week for four weeks for evaluating efficacy (Kamm et al., 2015) (van Beek et al., 2019a) (van Beek et al., 2020) (van Beek et al., 2022). Being primarily a feasibility study, we however shortened the training period to two weeks, however with high intensity.

Six different training exercises were developed with the goal to address different key functions of the hand/arm from finger to full arm movements. In this regard, the training exercises especially covered "pinch grip", "bending/stretching/circling fingers", "wrist rotation", "target-orientated finger" and "target-orientated full arm movements" as summarized as follows and illustrated in Fig. 2.

Training exercises:

1. Catching apples
2. Finger circling (Index finger)
3. Bending/stretching fingers
4. Pinch grip
5. Tracing shapes
6. Wrist rotation

Overall, ten training session were planned within two weeks, with the first of these sessions being supervised at baseline in the hospital within the instruction. The following nine training sessions at home were unsupervised. It was recommended to perform all six training exercises each training session in random order. Overall, a training session lasted approximately 20 minutes. All training exercises were performed in a seated position to avoid falls and injury, and the participants' hands were used to conduct all training programs through hand/finger

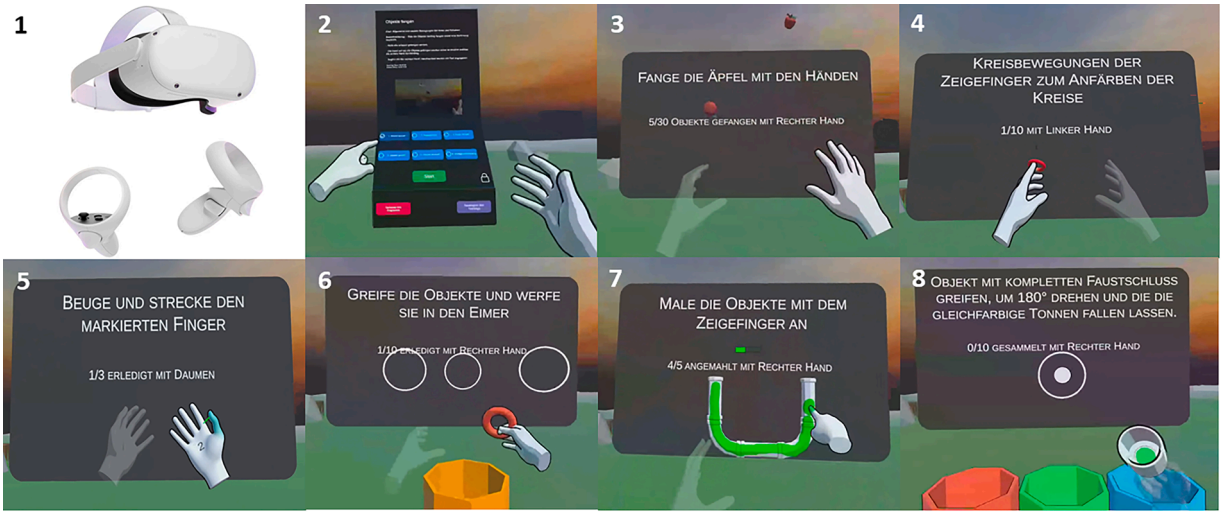

Fig. 2. Virtual reality headset-based immersive training intervention. Six trainings were specifically developed for this project on the Oculus quest 2 (Meta) addressing different hand/arm key functions. 1: Oculus quest 2; 2: Menu/Program overview. Training interventions (blue buttons) can be selected, and an instructional text and video is shown. Training is started pressing the green (Start) button; 3-8: Training interventions: 3: Catching apples; 4: Finger circling (Index finger); 6: Bending/stretching fingers; 6: Pinch grip; 7: Tracing shapes; 8: Wrist rotation. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

tracking technology and both hands were trained in each exercise in alternating fashion (one or the other hand).

2.4. Statistical Analyses

All statistical analyses were performed using Statistical Package for Social Science (SPSS) for Windows, version 27.0; SPSS; Inc. Chicago, IL, USA. The level of significance was set at $p < 0.05$. Descriptive statistics were used to present baseline and clinical characteristics. Non-parametric Friedman's ANOVA were done to compare observations (T0 = Visit 1: Screening/Baseline; T1 = Visit 2: Start Training; T2 = Visit 3: End Training/Study) for all outcome measures (presented as median score and Interquartile ranges, IQR) on the same subjects. With regard to efficacy of the training intervention, secondary outcome parameters before and after the training intervention (T1/T2) were compared to changes of secondary outcome parameter before and after the waiting period without training (T0/T1). Post-hoc Dunn-Bonferroni-Tests were done to compare single observations (T0 vs T1, T0 vs T2, T1 vs T2). The effect sizes of the individual comparisons were calculated. In this regard, the effect size of the Dunn-Bonferroni-test was calculated, which corresponds to the effect size of a rank sum test, r. The classification by Cohen (1992) was used to assess the magnitude of the effect size (r = .10 corresponds to a weak effect; r = .30 corresponds to a medium effect; r = .50 corresponds to a strong effect). Furthermore, we conducted Spearman correlational analyses between usability/adherence scores and demographic and clinical baseline characteristics to analyze a possible impact of these characteristics on usability/adherence.

3. Results

From April to July 2022, fifteen pwMS were asked to participate and eleven pwMS started and completed the study. Four pwMS declined because they did not want to participate in a study. No adverse events or dropouts were reported. Detailed clinical and demographic characteristics of the study cohort are presented in Table 1. There were no additional medication or diseases relevant to the study.

3.1. Feasibility

The adherence to the training protocol was good. Participants completed on average 8.18 sessions ± 1.88 (Standard Deviation (SD)) of the planned 10 sessions, being 81.8%.

Table 1
Demographic and clinical characteristics (n=11).

Age (y)	49.20 ± 10.87
Gender, n (%)	
female	7 (64)
male	4 (36)
Handedness, n (%)	
Right	11 (100)
Left	0 (0)
Disease duration (y)	15.38 ± 9.95
EDSS	4.28 ± 1.48
SDMT	44.64 ± 14.49
MS type, n (%)	
RRMS	9 (82)
SPMS	1 (9)
PPMS	1 (9)
Immunomodulatory therapy, n (%)	
Natalizumab	8 (73)
Ocrelizumab	2 (18)
Rituximab	1 (9)
VR-Experience, n (%)	
No	11 (100)

Values are mean ± SD or as otherwise indicated; SD, standard deviation; y, years; n, number of patients; EDSS, Expanded Disability Status Scale; RRMS, relapsing remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis; PPMS, primary progressive multiple sclerosis; VR-Experience, Experience with Virtual Reality headset before study participation.

Regarding the influence of baseline and disease characteristics on feasibility, a higher score in the CRT, in terms of more dexterous difficulties, significantly correlated with a higher adherence/feasibility (Spearman's rho -.781, p<0.01) whereas the other parameters did not (Table 2).

3.2. Usability

The median SUS score was very high being 94 (IQR = 78-96). Regarding the influence of baseline and disease characteristics on usability, the EDSS showed a significant correlation with higher EDSS scores corresponding to a reduced usability (Spearman's rho -.715, p=0.013). All other parameters including gender showed no significant correlations (Table 2). In addition, usability and feasibility did not

Table 2
Influence of Baseline characteristics on Feasibility and Usability.

	Age	Disease duration	EDSS	SDMT	9HPT (D)	9HPT (ND)	CRT (D)	CRT (ND)	AMSQ	JAMAR (D)	JAMAR (ND)
Feasibility	.005	.526	.119	-.435	.540	.165	.781**	.613*	.133	-.039	-.202
SUS	-.077	.119	-.715*	.361	-.533	-.300	-.452	-.533	-.507	.340	.065

Values are presented as Spearman's rho, *p<0.05; **p<0.01; EDSS, Expanded Disability Status Scale; SDMT, Single Digit Modality Test; 9HPT, Nine-Hole Peg Test; CRT, Coin Rotation Task; AMSQ, Arm Function in Multiple Sclerosis Questionnaire; JAMAR, handheld JAMAR dynamometer, D, dominant hand; ND, non-dominant hand

influence each other.

3.3. Patient engagement and satisfaction

Questions 1 to 5 of the CUEQ were rated high with median scores of 3 to 5, corresponding to "good", "very good" or "excellent". Questions 6 and 7 were rated lower, with a median score of 2 corresponding to "poor" (Fig. 3).

The overall rating of the training intervention was very high with a median VAS score of 8 (IQR = 7-9) on a scale from 1-10.

The individual written free-text feedback was overall very positive. Regarding improvements of the VR training, some pwMS suggested individual adjustments of the level of difficulty, incentives such as "reaching a new level" or "collecting points" for motivation, and more different trainings. In addition, participants gave practical suggestions for further development and raised technical issues.

3.4. Efficacy

There were no significant changes for all outcomes during the waiting period between Visit 1 (T0, Baseline) and Visit 2 (T1, Start of Training) (Table 3).

After the training intervention (Visit 3), the AMSQ scores did not significantly change, $\chi^2_{(2)} = 2.64$, $p = 0.27$. Similarly, the 9HPT, JAMAR, CRT (non-dominant hand), and MSIS scores did not significantly change ($9HPT_{dominant\ hand}$ $\chi^2_{(2)} = 3.80$, $p = 0.15$, $9HPT_{non\text{-}dominant\ hand}$ $\chi^2_{(2)} = 0.16$, $p = 0.92$, $JAMAR_{dominant\ hand}$ $\chi^2_{(2)} = 4.90$, $p = 0.09$, $JAMAR_{non\text{-}dominant\ hand}$ $\chi^2_{(2)} = 0.05$, $p = 0.97$, $CRT_{non\text{-}dominant\ hand}$ $\chi^2_{(2)} = 1.00$, $p = 0.61$, $MSIS_{total}$ $\chi^2_{(2)} = 0.86$, $p = 0.71$, $MSIS_{physical}$ $\chi^2_{(2)} = 0.55$, $p = 0.76$, $MSIS_{psychological}$ $\chi^2_{(2)} = 1.77$, $p = 0.41$).

There was a signifcant improvement for the CRT of the dominant hand, $\chi2(2) = 6.87$, $p = 0.03$. This signifcant improvement was related to change from Start to End of Training, $Z = 0.91$, $p = 0.03$, with a medium effect size ($r = 0.3$) (Table 3).

4. Discussion

This study aimed to evaluate the feasibility, usability and patient engagement/satisfaction of a new immersive home-based VR headset-based dexterity training in pwMS. To do so, a heterogenic cohort of pwMS was recruited with an age range of 23-65 years and an EDSS range from 0-6 (Table 1). None of the participants had experience with VR devices prior to study entry.

The feasibility of the training intervention was good with a high adherence to the training protocol (81.8%), which is further supported by the absence of adverse effects or dropouts.

Baseline and disease characteristics such as age, disability or cognition did not negatively affect feasibility which is important because manual dexterity is more pronounced in more disabled patients (Johansson et al., 2007). Interestingly, pronounced impaired manual dexterity measured by the CRT was correlated with a higher adherence. This could be due to a higher motivation of patient with dexterous difficulties, which would be positive regarding this training approach.

The usability of the training intervention was very high with a SUS score of 94 (IQR = 78-96). This result is reflected by the high overall rating of the training intervention with a median of 8 on the VAS.

Again, most baseline and disease characteristics did not influence usability which is important regarding realizations of such training interventions in patients with impaired manual dexterity. However, general disability measured with the EDSS impaired usability which must be considered in the further development of VR headset-based training interventions, for example with a more profound instruction of the training intervention in more disabled patients (Table 2). Usability, examined by the SUS, covered the use of the Oculus quest 2 and the training intervention, however with a clear focus on the training intervention. Handling of the Oculus quest 2 did not present a relevant

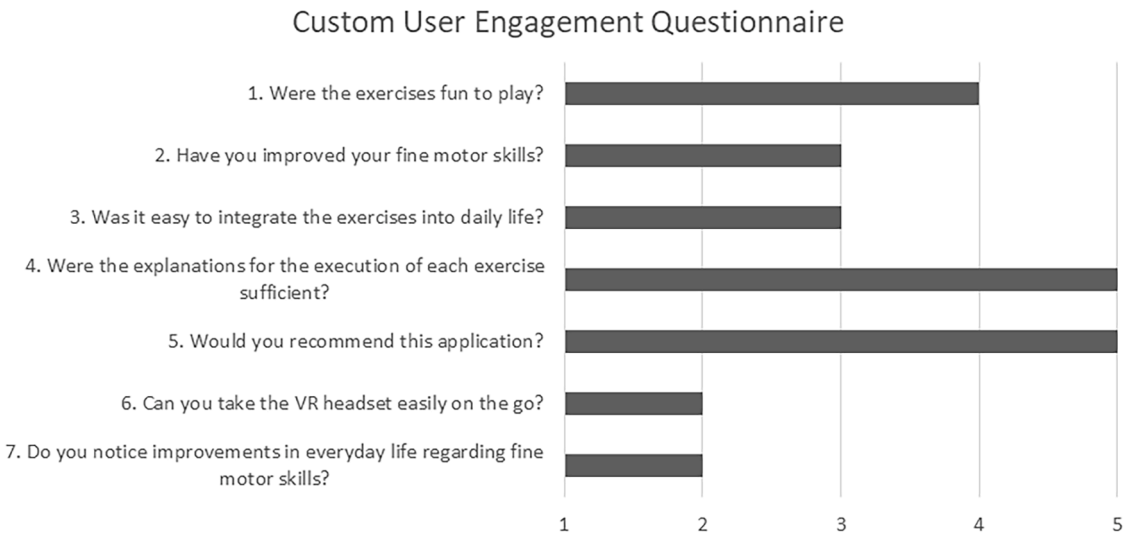

Fig. 3. Results of the Custom User Engagement Questionnaire (CUEQ). Seven questions related to the content of the Virtual Reality headset-based training intervention are scored on a scale ranging from 1 ("bad") to 5 ("excellent"). Median values are shown.

Table 3
Endpoints at baseline, start and end of training.

	baseline	Start Training	End Training	Friedman's test, p-value
AMSQ	32.00 (31.00-45.00)	33.00 (31.00-45.00)	33.00 (31.00-53.00)	0.27
9HPT				
dominant	19.50 (17.00-20.50)	20.00 (16.00-22.00)	17.50 (16.00-20.50)	0.15
non-dominant	21.00 (18.50-26.00)	21.00 (18.40-26.00)	21.00 (17.00-23.50)	0.92
JAMAR				
dominant	35.00 (29.50-47.50)	34.50 (27.00-47.00)	37.00 (27.00-46.00)	0.09
non-dominant	32.00 (28.50-43.00)	34.00 (26.00-39.00)	33.00 (29.00-41.00)	0.97
CRT				
dominant	15.50 (14.00-18.00)	15.00 (14.00-18.50)	14.00 (10.50-15.00)	**0.03***
non-dominant	18.00 (13.00-23.50)	18.00 (14.00-22.00)	15.50 (13.00-22.00)	0.61
MSIS-29				
Total	38.00 (34.00-56.00)	37.00 (34.00-45.00)	40.00 (33.00-52.00)	0.71
physical	26.00 (23.00-44.00)	26.00 (24.00-35.00)	28.00 (24.00-40.00)	0.76
Psychological	12.00 (11.00-14.00)	11.00 (10.00-12.00)	11.00 (10.00-15.00)	0.41

Values are presented as median with the 25th and 75th percentiles (IQR), Abbreviations: AMSQ = Arm Function in Multiple Sclerosis Questionnaire; 9HPT, Nine-Hole Peg Test; CRT, Coin Rotation Test; MSIS-29, Multiple Sclerosis Impact Scale.
*Dunn Bonferroni Post Hoc test difference between Start and End of Training, z = 0.86, p = 0.04 (effect size $r = 0.3$), between Baseline und End of Training, z = 0.91, p = 0.03 (effect size $r = 0.3$). No significant difference between Baseline and Start of training, p = 0.92.

problem in our cohort as most of the feedback was related to the training intervention and should become a lesser problem in the future if VR devices are increasingly used in daily life. Importantly, usability did not influence adherence rate in our study which means that despite subjective problems in using the device, the training intervention could be performed properly.

User engagement and satisfaction with the training intervention was good. The training intervention could be implemented well into everyday life, was fun, and participants would highly recommend it to other pwMS (Fig. 3).

Participants enjoyed the training intervention and found the approach interesting and innovative which are positive signs for the therapeutic use of VR headset devices in general and especially at home. Regarding the feedback, the training intervention could be improved by adjusting the level of difficulty to patient's performance, incentives such as "reaching a new level" or "collecting points" for motivation, and more different trainings. This valuable feedback will be implemented in upcoming training interventions.

Research on feasibility and usability of immersive VR headset-based dexterity training in pwMS is sparse and most published studies had a non-immersive hospital-based approach often using commercial games (Webster et al., 2021). Research on using specifically developed or adapted immersive VR interventions was performed as well in a supervised setting (Hollywood et al., 2022) (Bertoni et al., 2022). Regarding home-based unsupervised settings, we however did not find corresponding literature to compare our result with.

One very recently published study examining a 4-weeks immersive upper limb VR training in pwMS, used the Oculus Rift in a hospital-based setting with a supervising physiotherapist. Usability, also rated with the SUS, was only moderate (45.9 ± 11.1), with lower scores assigned to items representing user-friendliness. The authors discuss that this might be critical when using VR-based trainings unsupervised like in home-based settings and that an adequate initial training of the system, which was not administered in their study since the training was fully supervised, could improve usability (Bertoni et al., 2022). In our study, participants were instructed in detail regarding the use of the VR device due to the home-based nature of the training and written instructions were handed out as well. In addition, usability was one key focus in the creation of the specifically developed training intervention. These aspects probably contributed to the excellent usability even in a population with no prior experience with VR devices.

Our study was not powered or designed to examine the effectiveness of this new VR dexterity training. However, after the training intervention, there was a significant improvement of the CRT of the dominant hand and positive trends of the JAMAR and 9HPT of the dominant hand in a population not considerably affected by impaired manual dexterity. This may hint to an efficacies training intervention, especially if performed more than 2 weeks. In a previous study we could for example show, that a 4-weeks conventional home-based dexterity training program significantly improved manual dexterity and dexterity-related ADL in pwMS (Kamm et al., 2015). A 4-weeks home-based, tablet- and app-based dexterity training was found to be effective in improving specific dimensions (finger movements and strength) in pwMS as well (van Beek et al., 2022).

In addition, the 4-weeks hospital-based immersive VR training on upper limb function published by Bertoni et al., 2022 showed a significant improvement in gross manual dexterity in the less affected limb which however did not translate into dexterity related improvements in ADL (Bertoni et al., 2022). Similarly, participants in our study noticed an improvement in manual dexterity after completing the training intervention with a median value of 3 in CUEQ question 2 (4 participants <3, 6 participants ≥ 3), however without a relevant positive impact on daily life (median value of 2 in CUEQ question 7) as well (Fig. 3).

5. Limitations

The main limitation is the small sample of participants. However, for piloting a new training, this is an adequate sample, as we previously showed (van Beek et al., 2019). A generalization regarding the diversity of all pwMS is however not possible. To evaluate feasibility, we recorded at which dates participants performed the training intervention. As it was a home-based study, participants were not supervised and therefore, the exact performance of the training intervention regarding which exercises were performed for how long, which hands were used, how many repetitions were made, is unknown. Measuring adherence and the performance of the training intervention more detailed (performed exercises, duration of exercising, hands used etc.) using the Oculus quest 2 is in principle possible and another strength of VR devices which will be addressed in future studies. In addition, VR devices could be used to evaluate efficacy outcome parameter as well and initial research in this regard was recently published (Craig et al., 2022; Jost, 2021).

6. Conclusion

This is the first study evaluating the feasibility and usability of a home-based immersive VR headset-based dexterity training in pwMS. Feasibility, usability, and patient engagement/satisfaction of the training intervention was very high qualifying this treatment approach for the use in home-based neurorehabilitation. In addition, the preliminary efficacy results hint to an efficacious training intervention

regarding improvements in manual dexterity and further randomized-controlled trials in this regard are warranted.

Declarations of Competing Interest

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References

Benedict, RH., et al., 2017. Multiple Sclerosis Outcome Assessments Consortium. Validity of the Symbol Digit Modalities Test as a cognition performance outcome measure for multiple sclerosis. Mult. Scler. 23 (5), 721–733. https://doi.org/10.1177/1352458517690821.

Bertoni, R., et al., 2022. Effects of immersive virtual reality on upper limb function in subjects with multiple sclerosis: A cross-over study. Mult. Scler. Relat. Disord. 65, 104004 https://doi.org/10.1016/j.msard.2022.104004.

Borsci, S., et al., 2009. On the dimensionality of the System Usability Scale: A test of alternative measurement models. Cogn. Process 10 (3), 193–197. https://doi.org/10.1007/s10339-009-0268-9.

Brooke, J., 1986. SUS - A Quick and Dirty Usability Scale. Digital Equipment Corporation, Maynard, MA, p. 27. https://hell.meiert.org/core/pdf/sus.pdf [accessed 2020-05-29].

Buckingham, G., 2021. Hand Tracking for Immersive Virtual Reality: Opportunities and Challenges. Front. Virtual. Real. 2, 728461 https://doi.org/10.3389/frvir.2021.728461.

Chruzander, C., et al., 2013. A 10-year follow-up of a population-based study of people with multiple sclerosis in Stockholm, Sweden: Changes in disability and the value of different factors in predicting disability and mortality. J. Neurol. Sci. 332, 121–127.

Craig, CM., et al., 2022. Can We Use the Oculus Quest VR Headset and Controllers to Reliably Assess Balance Stability? Diagnostics (Basel) 12, 1409. https://doi.org/10.3390/diagnostics12061409.

Declaration of Helsinki (https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects) 2023.

Doumas, I., et al., 2021. Serious games for upper limb rehabilitation after stroke: a meta-analysis. Neuroeng. Rehabil. 18 (1), 100. https://doi.org/10.1186/s12984-021-00889-1.

Garrett, B., et al., 2018. Virtual Reality Clinical Research: Promises and Challenges. JMIR Serious Games 6, e10839. https://doi.org/10.2196/10839.

Giovannoni, G., et al., 2017. Is multiple sclerosis a length-dependent central axonopathy? The case for therapeutic lag and the asynchronous progressive MS hypotheses. Mult. Scler. Relat. Disord. 12, 70–78. https://doi.org/10.1016/j.msard.2017.01.007.

Heldner, MR., et al., 2014. The Coin Rotation Task: A Valid Test for Manual Dexterity in Multiple Sclerosis. Phys. Ther. 94, 1644–1651.

Hollywood, RA., et al., 2022. Proof of Concept for the Use of Immersive Virtual Reality in Upper Limb Rehabilitation of Multiple Sclerosis Patients. Adv. Exp. Med. Biol. 1356, 73–93. https://doi.org/10.1007/978-3-030-87779-8_4.

Johansson, S., et al., 2007. High concurrent presence of disability in multiple sclerosis. Associations with perceived health. J. Neurol. 254, 767–773.

Jost, TA., 2021. Quantitative analysis of the Oculus Rift S in controlled movement. Disabil. Rehabil. Assist. Technol. 16, 632–636. https://doi.org/10.1080/17483107.2019.1688398.

Kalkers, NF., et al., 2021. Differential item functioning of the Arm function in Multiple Sclerosis Questionnaire (AMSQ) by language, a study in six countries. Mult. Scler. 27 (1), 90–96. https://doi.org/10.1177/1352458519895450.

Kamm, CP., et al., 2014. Multiple Sclerosis: Current Knowledge and Future Outlook. Eur. Neurol. 72, 132–141. https://doi.org/10.1159/000360528.

Kamm, CP., et al., 2015. Mult. Scler. 21 (12), 1546–1556. https://doi.org/10.1177/1352458514565959.

Kobelt, G., et al., 2017. European Multiple Sclerosis Platform. New insights into the burden and costs of multiple sclerosis in Europe. Mult. Scler. 23, 1123–1136. https://doi.org/10.1177/1352458517694432.

Kurtzke, JF, 1983. Rating neurologic impairment in multiple sclerosis: An Expanded Disability Status Scale (EDSS). Neurology 33, 1444–1452.

McGuigan, C., Hutchinson, M., 2004. The multiple sclerosis impact scale (MSIS-29) is a reliable and sensitive measure. J. Neurol. Neurosurg. Psychiatry. 75, 266–269.

Oxford Grice, K., et al., 2003. Adult norms for a commercially available Nine Hole Peg Test for finger dexterity. Am. J. Occup. Ther. 57, 570–573.

Peolsson, A., et al., 2001. Intra- and inter-tester reliability and reference values for hand strength. J. Rehabil. Med. 33, 36–41.

Řasová, K., et al., 2020. Content and Delivery of Physical Therapy in Multiple Sclerosis across Europe: A Survey. Int. J. Environ. Res. Public. Health. 17, 886. https://doi.org/10.3390/ijerph17030886.

Steinheimer, S., et al., 2018. The Arm Function in Multiple Sclerosis Questionnaire was successfully translated to German. J. Hand. Ther. 31 (1), 137–140. https://doi.org/10.1016/j.jht.2017.09.010 e1.

Thompson, A., et al., 2016. Importance of upper limb function in advanced multiple sclerosis. Mult. Scler. 22 (suppl 3), P1277, 676.

Thompson, AJ., et al., 2018. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet. Neurol. 17 (2), 162–173.

van Beek, JJW., et al., 2022. Tablet App-Based Dexterity Training in Multiple Sclerosis (TAD-MS): a Randomised Controlled Trial. Disabil. Rehabil. Assist. Technol. Accept. https://doi.org/10.1080/17483107.2022.2131915.

van Beek, JJW., et al., 2019a. Tablet App Based Dexterity Training in Multiple Sclerosis (TAD-MS): Research Protocol of a Randomized Controlled Trial. Front. Neurol. 11 (10), 61. https://doi.org/10.3389/fneur.2019.00061.

van Beek, JJW., et al., 2019b. Exergaming-Based Dexterity Training in Persons With Parkinson Disease: A Pilot Feasibility Study. J. Neurol. Phys. Ther. 43 (3), 168–174. https://doi.org/10.1097/NPT.0000000000000278.

van Beek, JJW., et al., 2020. Feasibility of a Home-Based Tablet App for Dexterity Training in Multiple Sclerosis: Usability Study. JMIR. Mhealth. Uhealth. 8 (6), e18204. https://doi.org/10.2196/18204.

Vanbellingen, T., et al., 2017. Usability of videogame-based dexterity training in the early rehabilitation phase of stroke patients: A pilot study. Front. Neurol. 8, 1–9. https://doi.org/10.3389/fneur.2017.00654.

Webster, A., et al., 2021. Upper limb rehabilitation interventions using virtual reality for people with multiple sclerosis: A systematic review. Mult. Scler. Relat. Disord. 47, 102610 https://doi.org/10.1016/j.msard.2020.102610.

Yancosek, KE., Howell, DJ., 2009. A narrative review of dexterity assessments. J. Hand. Ther. 22, 258–269.

Yeroushalmi, S., et al., 2022. Telemedicine and multiple sclerosis: A comprehensive literature review. J. Telemed. Telecare. 26, 400–413. https://doi.org/10.1177/1357633X19840097.

Yozbatiran, N., et al., 2006. Motor assessment of upper extremity function and its relation with fatigue, cognitive function and quality of life in multiple sclerosis patients. J. Neurol. Sci. 246, 117–122.