Towards Effective Telerehabilitation: Assessing Effects of Applying Augmented Reality in Remote Rehabilitation of Patients Suffering from Multiple Sclerosis

MAGDALENA PRUSZYŃSKA*, Department of Orthopedic and Post Traumatic Rehabilitation, Medical University of Łódź, Poland
MARTA MILEWSKA-JĘDRZEJCZAK*, Department of Neurology and Stroke, Medical University of Łódź, Poland
IGOR A. BEDNARSKI, Department of Neurology and Stroke, Medical University of Łódź, Poland
PIOTR SZPAKOWSKI, Department of Neurology and Stroke, Medical University of Łódź, Poland
ANDRZEJ GŁĄBIŃSKI, Department of Neurology and Stroke, Medical University of Łódź, Poland
SŁAWOMIR K. TADEJA, Institute of Applied Computer Science, Jagiellonian University, Poland

Multiple Sclerosis (MS) is a chronic, incurable disease of the central nervous system that is also one of the most common causes of disability among young adults. Despite available pharmacological treatments, the patients often require ongoing, supervised rehabilitation. Thus, therapists are constantly searching for new, effective ways of improving functional performance and quality of life without frequently visiting medical centers. One of the most promising methods is remote telerehabilitation enhanced with an immersive augmented reality (AR) interface. Here, we investigated the effectiveness of using a commercially available AR system in MS patients' treatment. To evaluate such an approach to rehabilitation, we conducted a medical study with 30 MS patients undergoing immunomodulatory treatment. In this study, we evaluated the influence on the patients' upper limbs' hand grip strength and efficiency of the patients' upper limbs. In addition, we also analyzed the level of neurotrophins to assess the potential impact of the training on the brain plasticity process. Our results show that rehabilitation enhanced with AR significantly improves the strength and efficiency of the patients' upper limbs. Furthermore, we further infer that AR-enhanced systems are a promising possibility of training without leaving home.

CCS Concepts: • **Human-centered computing → Empirical studies in accessibility**; *Interactive systems and tools*; • **Applied computing → Health informatics**.

Additional Key Words and Phrases: augmented reality, mixed reality, telerehabilitation, multiple sclerosis, neuroplsticity

---

Authors' addresses: Magdalena Pruszyńska, magdalena.pruszynska@umed.lodz.pl, Department of Orthopedic and Post Traumatic Rehabilitation, Medical University of Łódź, Plac Hallera 1, Łódź, 91-647, Poland; Marta Milewska-Jędrzejczak, marta.milewska@umed.lodz.pl, Department of Neurology and Stroke, Medical University of Łódź, Żeromskiego 113, Łódź, 90-549, Poland; Igor A. Bednarski, igor.bednarski@umed.lodz.pl, Department of Neurology and Stroke, Medical University of Łódź, Żeromskiego 113, Łódź, 90-549, Poland; Piotr Szpakowski, piotr.szpakowski@umed.lodz.pl, Department of Neurology and Stroke, Medical University of Łódź, Żeromskiego 113, Łódź, 90-549, Poland; Andrzej Głąbiński, andrzej.glabinski@umed.lodz.pl, Department of Neurology and Stroke, Medical University of Łódź, Żeromskiego 113, Łódź, 90-549, Poland; Sławomir K. Tadeja, slawomir.tadeja@uj.edu.pl, Institute of Applied Computer Science, Jagiellonian University, Gołębia 24, Kraków, 31-007, Poland.

0004-5411/2022/8-ART0 $15.00
https://doi.org/00.000

ACM Reference Format:
Magdalena Pruszyńska, Marta Milewska-Jędrzejczak, Igor A. Bednarski, Piotr Szpakowski, Andrzej Głąbiński, and Sławomir K. Tadeja. 2022. Towards Effective Telerehabilitation: Assessing Effects of Applying Augmented Reality in Remote Rehabilitation of Patients Suffering from Multiple Sclerosis. *J. ACM* 0, 0, Article 0 (August 2022), 15 pages. https://doi.org/00.000

1 INTRODUCTION

Multiple sclerosis (MS) is a chronic, autoimmune disease of the central nervous system. MS commonly occurs in patients between the ages of 20 and 40, of which females suffer from two to three times more often than males [11]. MS is a global disease with its highest prevalence in Western Europe, North America, and Australasia, with an incidence greater than 100 per 100,000 inhabitants [12]. The most common subtype of MS is relapsing-remitting multiple sclerosis (RRMS), accounting for approximately 85% of all cases. The illness leads to progressive physical and mental disability. The most common deficits in the course of MS include motor disability, visual impairment, cognitive decline, and sphincter disorders [11]. All these ailments lead to progressive limitations in everyday functioning, professional absenteeism, and social exclusion. Thus, even the slightest amelioration of the patient's health or mitigation of the MS symptoms can bring a tremendous amount of comfort and relief.

Apart from the available pharmacological treatment, specialist rehabilitation plays an essential role in the treatment process. The use of an appropriately selected set of exercises can lead to the improvement of motor skills as well as limited recovery of cognitive functions by inducing neuronal plasticity [25]. However, traditionally, patient rehabilitation takes place in hospitals and other medical facilities under the constant supervision of a physiotherapy expert. Due to limited healthcare resources additionally constrained by pandemic prevention regulations limiting access to in-person therapy, sustaining such an approach is challenging, especially with the continuously growing number of people suffering from MS [50]. Therefore, it is critical to carry patient training outside of the clinic environment, which in turn, can expedite the rehabilitation process [47].

As a result, medical researchers and practitioners are constantly looking for new tools in slowing down disability caused by MS. Here, one of the relatively unknown, yet, already promising methods is the usage of so-called *telerehabilitation* in MS treatment [29]. The term itself encompasses various technologies used to conduct parts of patients' rehabilitation using telecommunication networks. Such remote rehabilitation program is consulted and assigned by a medical practitioner who supervises and tracks the patient's progress online with the help of an electronic feedback system [45]. Recently, one of the newest waves of such systems is enhanced with immersive interfaces such as augmented reality (AR) [39, 43, 44]. AR is a technology that allows for blending digital artifacts into the user's field of view. Such digital objects can be interacted with in many ways, including gaze-tracking, hand-tracking, and gesture recognition.

To this end, in this work, we are using commercially available technology to assess the effects of applying an AR-based interface in the remote rehabilitation of MS patients. We used the *Neuroforma*[1] AR system, in which the user sees a real-time reflection on the screen. This view is augmented with additional digital artifacts (see Fig. 1–2). Such an approach to realizing the AR interface, although not yet common, is currently an active field of research [27]. The system can track the user's gestures and detect whether and how the user engaged with the system. Thus, allowing for the tracking of the therapy's progress. The physiotherapist remotely supervising the rehabilitation process sets an individual rehabilitation program, i.e., selects the type and number of exercises, the number of rounds (exercise time), and the range of motion. In the online version of the system, the

[1]https://www.neuro-forma.com/

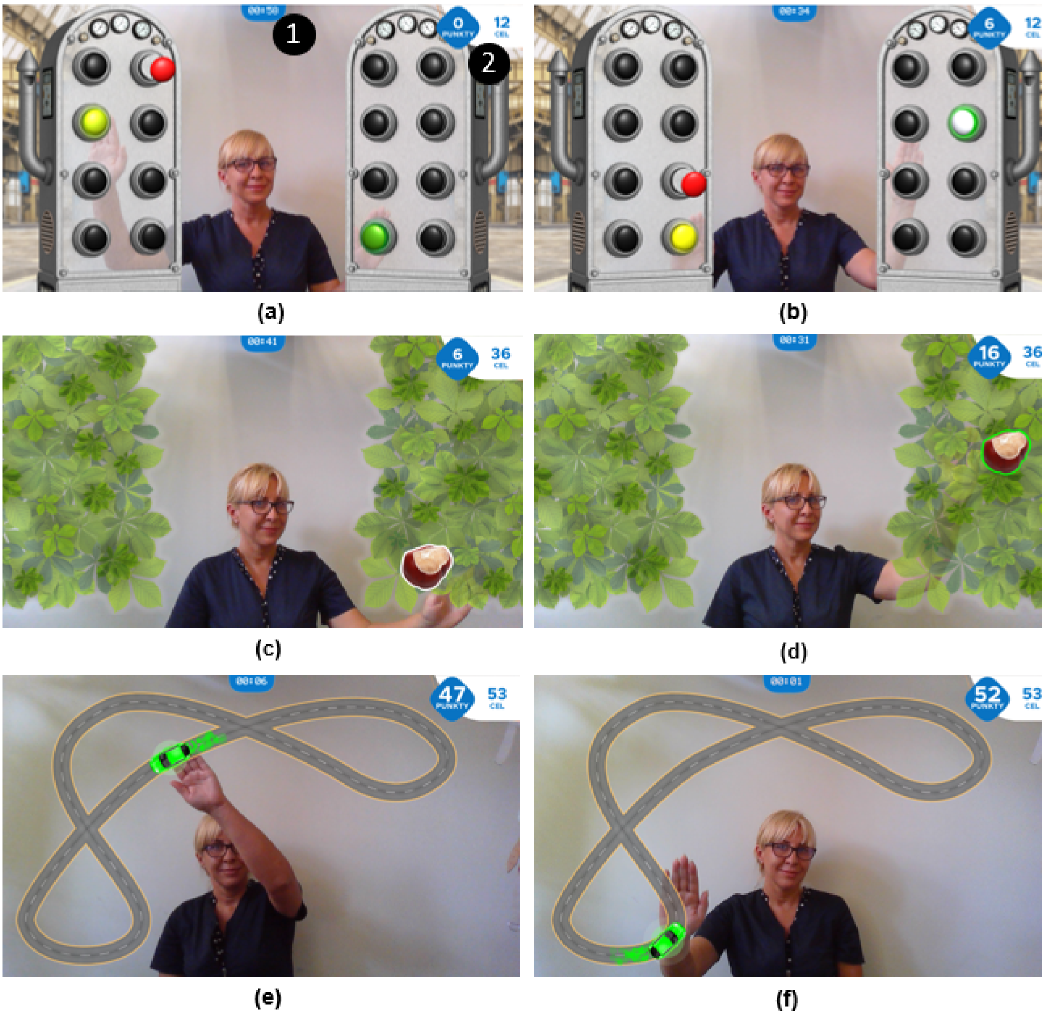


Fig. 1. (a-b) *Machine:* The patient has to press the white lights. When tapped with both hands, the lights turn green, whereas it turns yellow if one light is touched, it turns yellow. The patient loses points when pressing the red light. This exercise is designed for bilateral, symmetrical, and asymmetrical movements of the upper limbs. In addition, (1) marks the exercise timer, whereas (2) shows the current patient's score. Both the timer and score are visible to the patients in each exercise. (c-d) *Chestnuts:* The patient collects chestnuts that appear on the screen. This exercise is designed for the training of upper limbs. (e-f) *Track:* The patient is following the car with one hand along the designated track, which is also an exercise designed for the rehabilitation of the upper limb.

physiotherapist receives a notification that the patient has not exercised for more than 48 hours and can send a reminder in the form of a text, sound, or video message. Both the patient and therapist receive an automatic email notification about the message being delivered. We used this system to carry out a clinical study, which confirmed the effectiveness and potential benefits of using AR-based systems in the rehabilitation of MS patients.

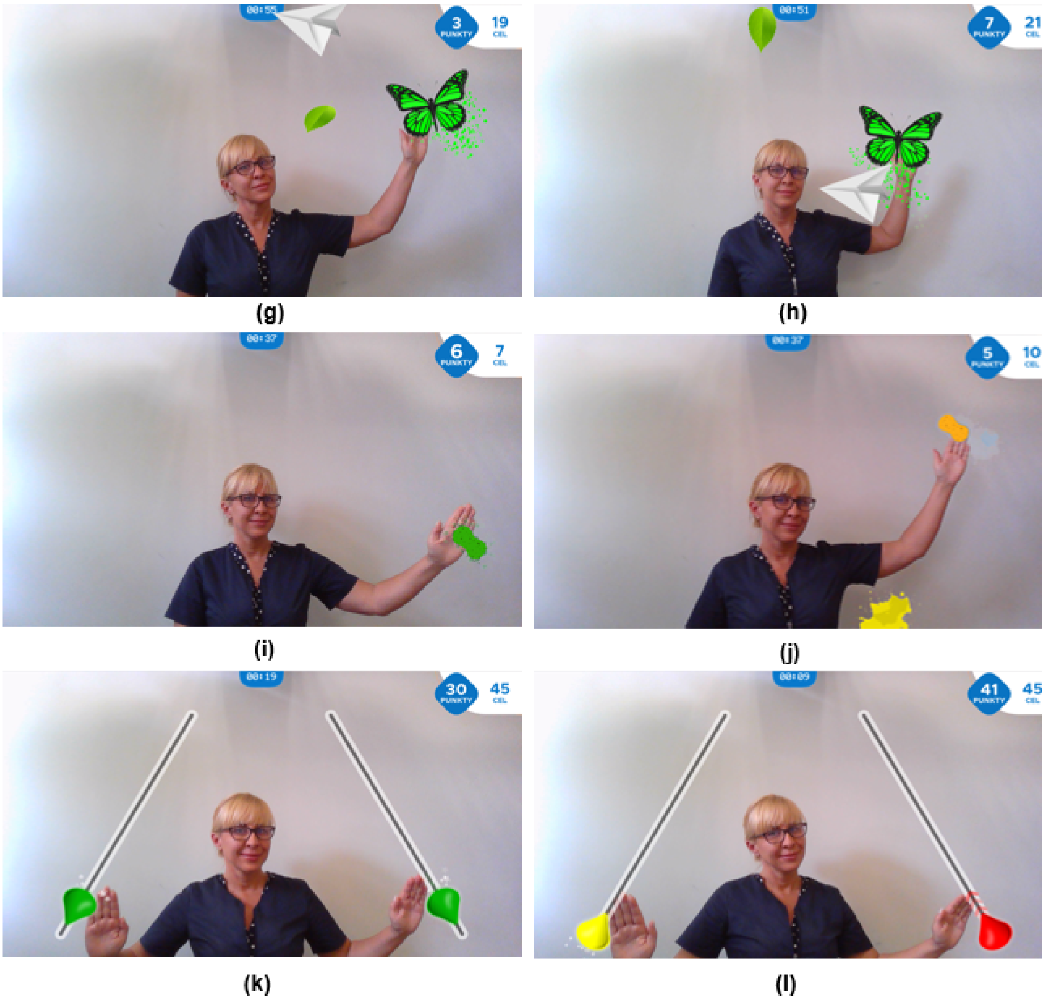


Fig. 2. These three exercises are also designed for upper limb training. (g-h) *Butterfly*: Here, the patient has to follow a butterfly with a single hand. (i-j) *Wiper* The patient wipes the stains with of the hands. (k-l) *Paths*: The patient follows the movement of balloons with both hands along the designated paths. If patients remove a hand from the corresponding balloon turns red, and when only one balloon is touched, it turns yellow.

2 RELATED WORK

The idea of rehabilitation carried out with the help of digital technologies is gaining traction and interest over the recent years [19, 39, 54]. Furthermore, the present-day mass-market adoption of the immersive technology brought new promise related to the application of such interfaces to patient rehabilitation [10, 38, 41]. Previous works often remark about the potential and advantages of immersive technology to provide tools, and environment for home-based rehabilitation [10, 45, 49]. The computer system can almost entirely supervise such a process, and an expert would periodically assess only the treatment results. Over the past two decades, there have been several studies concerning telerehabilitation facilitated with immersive interfaces.

For instance, an AR-based system for hand movement rehabilitation was proposed by Shen et al. [43, 44]. Here, the authors used gloves for the acquisition of patients data, whereas the AR interface provided visual feedback and additional stimuli to the patients. A specially designed glove was also used by Lipovský et al. [28] for the self-hand rehabilitation process. Other authors [1, 26] used Virtual Reality (VR) as a means of upper limb prosthetic rehabilitation. There are many more examples of immersive interfaces [3, 31, 45] being used in the recovery of motor functions of the patient's upper limbs, which typically involve some form of arm stretching and grabbing [28, 45]. Similar approaches were used in the case of stroke which was another frequently researched subject [8, 15, 18–22, 28, 40, 45, 46, 48].

Other fields of immersive interfaces applications were rehabilitation in cerebral vascular accident (CVA) [2, 47], cerebral palsy [6, 9] and even rare diseases [17].

Relatively little, however, has been done to date regarding the treatment of patients with MS by the means of immersive technologies. One example of a such system for MS rehabilitation was given by Lozano-Quilis et al. [30]. Their REMOVIEM system used the Microsoft Kinect for tracking the patient's movements when conducting exercises. However, the paper did not include the results of the planned user studies. The Kinect was also used as means of interaction by Desai et al. [10] researching game-based exercise in rehabilitation. Here, the usability and playability of the developed solution were tested in a small qualitative study with healthy adults. The results of this study were in favor of the exergames approach to rehabilitation. In addition, both these papers discussed and motivated the selection of particular exercises and commented on the feasibility of using exergames in rehabilitating patients suffering from MS and other forms of motor disabilities [10, 30]. In contrast to these prior works, we had carried out and reported on the results of a qualitative clinical trial study involving MS patients undergoing treatment. In addition, the Neuroforma system used in our study does not rely on Kinect or any other separate trackers.

3 EXPERIMENTS

3.1 Rehabilitation in Augmented Reality

The patients from the study group exercised at home for four weeks, five times a week with twenty specially designed treatment sessions in total. Each session lasted between 40 to 45 minutes per day. There was also the possibility for the patient to take breaks during the exercise. On the monitor, the patient is able to see the mirror image streamed from a camera overlaid with virtual objects (see Fig. 1–2). The patient's task is to move to designated points or follow a virtual object, e.g. along designated paths (see Fig. 1–2). The user also receives additional visual and audio feedback informing them whether they are completing the tasks properly. Before each exercise, the correct posture and setting of the patient are verified. However, if the automatic calibration fails, the exercise will be started anyway.

All patients received the same set of eight exercises related to the function of the upper limb (see example tasks in Fig. 1–2). Each of these exercises had to be performed for at least 4 minutes. Two of the planned tasks *Butterfly* and *Wiper* were designed especially for unilateral arm movement of the weaker limb as seen in Fig. 1(g-h) and Fig. 1(i-j) respectively. Whereas the remaining exercises were designed to be performed using bilateral arm movement. For safety reasons, e.g., no physiotherapist protection, the patients performed all exercises in a sitting position. The system automatically sent online the reports from the exercise session to the supervising medical expert.

3.2 Participants

We recruited the participants from the Department of Neurology and Stroke at the University Clinical Hospital Military Memorial Medical Academy - Central Veterans' Hospital of Łódź. Out of

Table 1. The clinical parameters measured during the course of the study with the statistically significant results marked in bold.

	Study group (N=15)	Control group (N=15)	p-value
Age (years)	38.33 ± 7.61	41.40 ± 4.61	0.1951
Age of MS diagnosis	30.07 ± 8.43	34.80 ± 5.56	0.0818
Disease duration (years)	9.93 ± 5.42	9.60 ± 4.34	0.8539
Female	11	11	
Male	4	4	

the 30 patients with RRMS enrolled in the study, 22 were female and 8 were male. Our inclusion criteria included the diagnosis of MS according to the 2010 McDonald criteria [37], currently receiving immunomodulating therapy (drugs like *glatiramer acetate, natalizumab, fingolimod, interferons, dimethyl fumarate*), no relapse of MS within 30 days before the commencement of the study, and finally, the possibility of giving written, informed consent to participate in the study.

On the other hand, the exclusion criteria were significant cognitive impairment, significant visual acuity impairment, simultaneous participation in another rehabilitation or medical experiment, and orthopedic disorders in the upper limbs that prevented participation in the study. Moreover, we excluded patients with muscle strength of the weaker upper limb with less than third grade level, i.e., the patient is able to actively move the limb against gravity, in accordance to the muscle strength scale Medical Research Council (MRC)[2].

In the study group, the mean age was 38.33 ± 7.61 years, the age at onset of MS was 30.07 ± 8.43 years, and the duration of the disease was 9.93 ± 5.42. Whereas, in the control group, the respective characteristics were as follows: 41.40 ± 4.61 was the mean of the ages of the patients, 34.80 ± 5.56, and 9.60 ± 4.34 were the means of the ages at the time of diagnosis of MS as well as the length of time since diagnosis of MS, respectively. As can be seen, the participants from both groups in the study did not differ significantly in terms of age, sex, and duration of symptoms. Detailed characteristics is shown in Tab. 1.

3.3 Experimental Design and Tasks

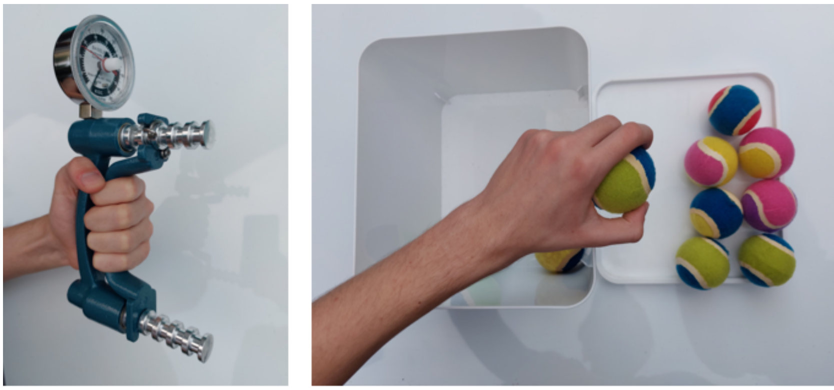
All the patients routinely visited the MS Outpatient Clinic once a month which is a standard procedure for their stages of MS. Our experiment was set up to cover the time between those routine appointments.

The patients included in the study group performed training with the use of AR for four consecutive weeks. They were provided with an online link to download and install the Neuroforma software on their personal computers and laptops. To be fully functional the system only required a camera as an input device and a screen to present AR content together with output of users movements.

Whereas, the participants in the control group did not undergo rehabilitation with the AR system. Instead, they were advised to exercise independently at home and to include both hands in everyday activities. Due to the SARS-CoV-2 epidemic, frequent visits to the clinic could be associated with a higher risk of infection. Therefore, it was not possible to monitor the correctness of the exercise performed by patients from the control group or even to confirm without a doubt that the patients did execute the assigned exercises.

The patients' upper extremity dexterity was evaluated while performing different tasks. In order to achieve this, we used the 9-hole peg test (9-HPT) protocol [24], in which the patient's task was

[2]https://mrc.ukri.org



(a) (b)

Fig. 3. (a) Measurement of the hand grip strength, and (b) re-movement of the balls from a box and placing them on the tray.

to individually remove 9 pegs from the container and insert them into the board with holes, and then remove and return the pegs to the container [34]. The 9-HPT is a standardized, quantitative assessment tool used to measure finger dexterity of patients with various neurological disorders, which we used to assess fine motor coordination (grasping of small objects). We designed a test with an easier to execute task of removing 10 balls related to the ability of catching balls one-by-one, maintaining a spherical grip, and placing the balls on the tray (see Fig. 3(b)). This test measured the upper limbs movement velocity in a greater range motion. This test could also be used for patients performing mass pattern movements i.e. able to control their spherical grasp even with limited functional use. In both tests, the patient was asked to complete the task as soon as possible. Additionally, handgrip strength, i.e., the isometric grip force in both hands, was measured with a hydraulic hand dynamometer (see Fig. 3(a)). The participants from both groups were asked to perform the tasks twice: at the time of commencement of the study and after the end of the four-week-long rehabilitation cycle. Additionally, we also collected 25 [ml] of venous blood from all the patients for the ethylenediamine tetraacetic acid (EDTA) anticoagulant diagnostic [4]. The blood was processed according to the standard laboratory procedure i.e., centrifuged at $1800xg$ at 20° Celsius for 15 minutes, the resulting plasma was aliquoted and stored at −80° Celsius. For protein expression analysis, we used commercially available ELISA kits in accordance with the protocol provided by the kits manufacturers for brain-derived nerotrophic factor (BDNF) and platelet-derived growth factor (PDGF) (R&D Systems).

All the study participants signed an informed consent form to participate in the experiment. The study was approved by the Bioethics Committee of the Medical University of Łódź[3].

3.4 Statistical Analysis

In order to conduct our study we followed the between-subject medical trial standard practice. Therefore, we randomly allocated the 30 MS patients into two groups: the control group with $N = 15$ individuals and the study group with another $N = 15$ individuals. Both groups had the same male to female ratio of 4/11.

We performed the group allocation using random permuted blocks. First, we created a randomization list with balanced allocation to treatment groups using six blocks with assigned ranks from

[3]Consent no RNN/172/17/KE of May 16, 2017

Table 2. The biochemical parameters measured during the course of the patients study. The data was log-transformed.

	Study group (N=15)			Control group (N=15)		
	before	after	p-value	before	after	p-value
BDNF	6.11 ± 0.87	5.86 ± 0.88	0.2535	6.05 ± 0.81	6.34 ± 0.50	0.0954
PDGF	7.25 ± 2.02	7.25 ± 0.70	0.6875	7.62 ± 0.89	7.62 ± 0.87	0.8668

1 to 6. Then, we used the pseudo-random number generator to allocate the first patient into the block. The subsequent three same-sex patients enrolled in the study were assigned to that block. After four patients, we repeated the procedure.

In Tab. 1, we present the means of the patients' characteristics including their respective ages, disease duration, and the ages of MS diagnosis. To compare differences between control and study groups we used the t-tests/non-parametric counterpart as well as the χ^2-test. Next, we compared task performance among the study groups before and after the patients underwent a four-week-long rehabilitation program using an AR system. We used a generalized linear model (GLM) with Tukey's post-hoc testing, to measure the differences between the control and study groups. The task execution time and neuromarker concentration were log-transformed. In all the tests we used the conservative value for $\alpha = 0.05$. We carried out the analyses with *Statistica* and *GraphPad Prism*.

3.5 Results

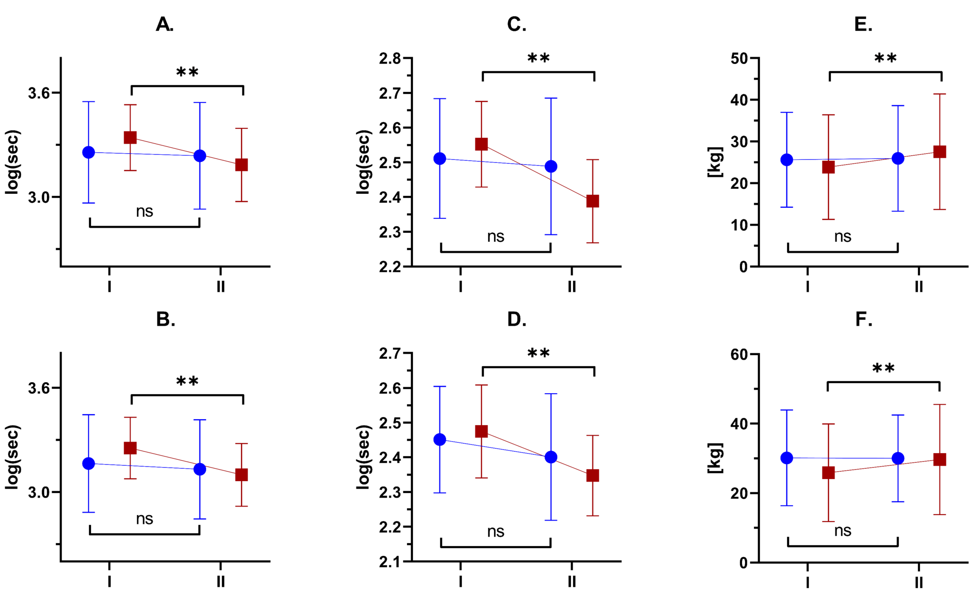


Fig. 4. The results of the statistical analysis. The asterisks mark the statistically significant results and the p-levels of $p \leq 0.01$. The tasks performances in the control (blue) and study groups (red). The data is shown as means with standard deviation (whiskers). A. 9-hole peg test in weaker site; B. 9-hole peg test in stronger site; C. Ball pulling test in weaker site; D. Ball pulling test in stronger site; E. Grip strength in weaker site; F. Grip strength in stronger site.

Table 3. Comparison of the tasks performance among the study and control groups. Statistically significant results were marked in bold and the time data was log-transformed.

Test	Group	Site	Before	After	p-value	Test power
9-hole peg test (sec.)	Study	Weaker	3.34±0.19	3.19±0.21	**0.0002**	0.5210
		Stronger	3.25±0.18	3.10±0.18	**0.0002**	0.6098
	Control	Weaker	3.26±0.29	3.24±0.31	0.7418	0.0537
		Stronger	3.16±0.28	3.13±0.29	0.2790	0.0593
Grip strength (kg)	Study	Weaker	23.87±12.54	27.53±13.86	**0.0002**	0.1157
		Stronger	25.87±14.03	29.67±15.86	**0.0009**	0.1050
	Control	Weaker	25.60±11.38	25.93±12.67	0.9608	0,0506
		Stronger	30.13±13.78	30.00±12.46	0.9987	0.0501
Ball pulling (sec.)	Study	Weaker	2.55±0.12	2.39±0.12	**0.0002**	0.9467
		Stronger	2.47±0.13	2.35±0.12	**0.0002**	0.7308
	Control	Weaker	2.51±0.17	2.49±0.20	0.7951	0.0597
		Stronger	2.45±0.15	2.40±0.18	0.0772	0.1283

Detailed results are shown in Tab. 2-3 as well as in Fig. 4. We observed no significant differences in concentration of BDNF and PDGF in both groups (see Tab. 2). In the 9-HPT there was significant decrease in execution times on both examined body sites (weaker and stronger) in the study group (from 3.34 ± 0.19 [sec] down to 3.19 ± 0.21 [sec], $p \leq 0.01$ for weaker site and from 3.25 ± 0.18 [sec] down to 3.10 ± 0.18 [sec], $p \leq 0.01$ for stronger site). On the other hand, we observed no such differences in the control group (see Fig. 4(A-B)).

Regarding the tasks of manual ball pulling, the study group performed significantly better (from 2.55 ± 0.12 [sec] down to 2.39 ± 0.12 [sec], $p \leq 0.01$ for weaker site and from 2.47 ± 0.13 [sec] down to 2.35 ± 0.12 [sec], $p \leq 0.01$ for stronger site). While the analysis of the control group results revealed no significant differences (see Fig. 4(C-D)). We also noted that in the study group there was a significant increase in grip strength (from 23.87 ± 12.5 [kg] up to 27.53 ± 13.86 [kg], $p \leq 0.01$ for weaker site and from 25.87 ± 14.03 [kg] up to 29.67 ± 15.86 [kg], $p \leq 0.01$ for stronger site). Whereas, we found no significant changes in the control group (see Fig. 4(E-F)).

Lastly, we have compared task performance and strength between examined sites (weaker and stronger) in the study group and found that there were no significant differences between weaker and stronger site for the 9-HPT ($p = 0.9$), ball pulling test ($p = 0.15$), as well as in observed grip strengths ($p = 0.91$).

4 DISCUSSION

The prior research concluded that the use of AR in rehabilitation had positive effects on the motor efficiency of the upper and lower limbs as well as the strength and gait in patients with neurological diseases [51–53].

In their reviews [32, 33], the authors remarked that digital exercise programs are a valuable and motivating component of patients therapy that could be successfully applied in the rehabilitation of patients with MS. At the same time, they emphasize that more research is needed as the prior work in this area is mostly characterized by poor methodological quality e.g., small numbers, no indication of the intensity of therapy, no control group, a varied or imprecise program of therapy.

In response to that need, this paper discusses the results of a medical trial with 30 patients suffering from MS. Our study investigated the feasibility of using AR-enhanced systems in MS patients' telerehabilitation. Based on this study results, we remark that the remote rehabilitation cycle carried out with the help of AR system had a positive effect on the strength and efficiency of the upper limbs of patients diagnosed with MS.

These improvements are likely related to the development of brain neuroplasticity via mirror neurons located in the motor cortex [14]. The activation of mirror neurons occurs as a result of performing an activity, but also during observation of an activity performed by another person [7]. In our study we did not find that using rehabilitation with immersive interface is related to significant changes in serum neurotrophin levels (BDNF, PDGF) which is consistent with current literature data [5, 35, 42]. However, a recent study with stroke patients undergoing 5-8 weeks long VR-based treatment coupled with standard therapy has revealed changes in their neuroplasticity [16]. The lack of observable findings may be related to the duration of our study, which in our case may be too short (4 weeks) to result in any noticeable effects and was not conjunct with regular occupational therapy.

In the current research, there are no similar studies assessing AR training with its effect on the level of plasma neurotrophins. Further work is required to evaluate other neurotrophins on their potential activity on brain plasticity. Thus far, our research is one of the first steps towards assessing the effectiveness of immersive interface in rehabilitation of MS patients in relation to plasma neurotrophins. Moreover, the observed improvements are of particular importance to patients as MS is currently considered incurable and the medical therapies are aimed to only delay or minimize the onset of symptoms or the development of the disease.

4.1 Limitations

The experimental results must be analyzed with caution as there were certain limitations imposed by the current epidemiological situation related to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). For instance, to minimize the potential contamination and spread of SARS-CoV-2, all the exercises were assigned to be carried out in the respective patients' houses. Due to this, only the patients from the study group that were using the immersive telerehabilitation systems were continuously monitored, as the system recorded and sent their individual exercise reports to the researchers. However, in the case of the control group, there was no possibility of tracking and supervising how the participant conducted their assigned tasks. Hence, the patients from the control group may have performed assigned exercises incorrectly, carried out an insufficient amount of task repetitions, or not exercised at all. As such, the results of the groups' comparison should be interpreted as the difference between the patients undergoing rehabilitation and those who did not undergone similar treatment. Furthermore, as we tracked the exercises execution in the study group, we can assess the progress of the patients using the remote AR rehabilitation system in comparison to the control group members.

Moreover, as MS is a heterogeneous disease with a fluctuating course, often depending on the individual patient [23]. Frequently, the clinical state of the disease is significantly different in patients of similar age, duration of MS symptoms, and similar radiological advancement of changes in the central nervous system [13]. This creates particular difficulties in selecting patients for the study and in the final evaluation of the results. Considering the fluctuating symptoms of MS, it seems necessary to reassess the patients after some time has passed.

5 CONCLUSION

Multiple sclerosis still remains an incurable disease, that leads to progressive physical and mental disability of patients. Besides the currently available medication, an important role in patients treatment is played by rehabilitation. A carefully designed and executed rehabilitation plan can result in an improvement of a patient's motor skills as well as the betterment of cognitive functions by inducing neuronal plasticity [25]. Recent work has shown, that changes in the concentration of brain plasticity biomarkers is responsible for further development of brain plasticity [36]. Recent results also suggest that an immersive environment such as VR can influence the levels of patients' neurothropins [16]. However, our analysis has shown no such changes among the MS patients undergoing AR-based treatment.

Since current treatment regimens can only delay or temporarily mitigate MS symptoms, it becomes even more important to determine which forms of therapy and rehabilitation could induce brain plasticity. Thus, slowing down the patient's disability is vital issue.

In this context, one of the relatively new, but already very promising methods is to apply immersive systems in MS patients' rehabilitation [32]. The use of remote immersive tools such as the one presented in this study, is particularly advantageous and convenient for patients with motor disabilities, as they can benefit from rehabilitation without having to leave their homes. Moreover, previous studies found that the use of immersion interfaces in rehabilitation, in particular in combination with gamification elements, has a positive effect on the development of patient involvement and motivation for further exercise [53]. In the life-long rehabilitation of the patients suffering from MS, their motivation and willingness to carry out assigned exercises can have a profound impact on their daily lives.

In conclusion, the results of our study indicate that the four-week telerehabilitation cycle conducted with an AR-enhanced system, improves the function of the upper limb and increases the handgrip strength, but does not increase the level of tested neurotrophins. Nonetheless, this form of therapy can be a valuable complement to a rehabilitation program aimed at improving the function of the upper limbs in patients with MS. However, to verify the effectiveness of this form of therapy, it is necessary to conduct further studies on a larger group of patients.

ACKNOWLEDGMENTS

We would like to thank Titanis Sp. z o.o. for allowing us to user their *Neuroforma*[4] platform to carry out the medical study. We would also like to thank Sergio Sanchez for proofreading the manuscript.

REFERENCES

[1] Adel Al-Jumaily and Ricardo A. Olivares. 2009. Electromyogram (EMG) Driven System Based Virtual Reality for Prosthetic and Rehabilitation Devices. In *Proceedings of the 11th International Conference on Information Integration and Web-Based Applications & Services* (Kuala Lumpur, Malaysia) *(iiWAS '09)*. Association for Computing Machinery, New York, NY, USA, 582–586. https://doi.org/10.1145/1806338.1806448

[2] Yee Mon Aung and Adel Al-Jumaily. 2011. Augmented Reality Based Reaching Exercise for Shoulder Rehabilitation. In *Proceedings of the 5th International Conference on Rehabilitation Engineering & Assistive Technology* (Bangkok, Thailand) *(i-CREATe '11)*. Singapore Therapeutic, Assistive & Rehabilitative Technologies (START) Centre, Midview City, SGP, Article 50, 4 pages.

[3] Yee Mon Aung and Adel Al-Jumaily. 2011. Development of Augmented Reality Rehabilitation Games Integrated with Biofeedback for Upper Limb. In *Proceedings of the 5th International Conference on Rehabilitation Engineering & Assistive Technology* (Bangkok, Thailand) *(i-CREATe '11)*. Singapore Therapeutic, Assistive & Rehabilitative Technologies (START) Centre, Midview City, SGP, 4 pages.

[4] Giuseppe Banfi, Gian Luca Salvagno, and Giuseppe Lippi. 2007. The role of ethylenediamine tetraacetic acid (EDTA) as in vitro anticoagulant for diagnostic purposes. *Clinical Chemistry and Laboratory Medicine* 45, 5 (2007), 565–576. https://doi.org/10.1515/CCLM.2007.110

[5] J. Bansi, W. Bloch, U. Gamper, and J. Kesselring. 2013. Training in MS: influence of two different endurance training protocols (aquatic versus overland) on cytokine and neurotrophin concentrations during three week randomized controlled trial. *Multiple Sclerosis Journal* 19, 5 (2013), 613–621. https://doi.org/10.1177/1352458512458605

[6] Emilia Biffi, Cristina Maghini, Alessia Marelli, Eleonora Diella, Daniele Panzeri, Ambra Cesareo, Chiara Gagliardi, Gianluigi Reni, and Anna Carla Turconi. 2016. Immersive VR Platform for Cerebral Palsy Rehabilitation. In *Proceedings of the 4th Workshop on ICTs for Improving Patients Rehabilitation Research Techniques* (Lisbon, Portugal) *(REHAB '16)*. Association for Computing Machinery, New York, NY, USA, 85–88. https://doi.org/10.1145/3051488.3051497

[4] www.neuroforma.pl

[7] Rocco Salvatore Calabrò, Antonino Naro, Margherita Russo, Antonino Leo, Rosaria De Luca, Tina Balletta, Antonio Buda, Gianluca La Rosa, Alessia Bramanti, and Placido Bramanti. 2017. The role of virtual reality in improving motor performance as revealed by EEG: a randomized clinical trial. *Journal of NeuroEngineering and Rehabilitation* 14, 1 (June 2017), 53. https://doi.org/10.1186/s12984-017-0268-4

[8] Yinpeng Chen, Nicole Lehrer, Hari Sundaram, and Thanassis Rikakis. 2010. Adaptive Mixed Reality Stroke Rehabilitation: System Architecture and Evaluation Metrics. In *Proceedings of the First Annual ACM SIGMM Conference on Multimedia Systems* (Phoenix, Arizona, USA) *(MMSys '10)*. Association for Computing Machinery, New York, NY, USA, 293–304. https://doi.org/10.1145/1730836.1730872

[9] Ana Grasielle D. Corrêa, Natália R. Kintschner, Victor Z. Campos, and Silvana M. Blascovi-Assis. 2019. Gear VR and Leap Motion Sensor Applied in Virtual Rehabilitation for Manual Function Training: An Opportunity for Home Rehabilitation. In *Proceedings of the 5th Workshop on ICTs for Improving Patients Rehabilitation Research Techniques* (Popayan, Columbia) *(REHAB '19)*. Association for Computing Machinery, New York, NY, USA, 148–151. https://doi.org/10.1145/3364138.3364169

[10] Kevin Desai, Kanchan Bahirat, Sudhir Ramalingam, Balakrishnan Prabhakaran, Thiru Annaswamy, and Una E. Makris. 2016. Augmented Reality-Based Exergames for Rehabilitation. In *Proceedings of the 7th International Conference on Multimedia Systems* (Klagenfurt, Austria) *(MMSys '16)*. Association for Computing Machinery, New York, NY, USA, Article 22, 10 pages. https://doi.org/10.1145/2910017.2910612

[11] Massimo Filippi, Amit Bar-Or, Fredrik Piehl, Paolo Preziosa, Alessandra Solari, Sandra Vukusic, and Maria A. Rocca. 2018. Multiple sclerosis. *Nature Reviews Disease Primers* 4, 1 (Nov. 2018), 43. https://doi.org/10.1038/s41572-018-0041-4

[12] GBD 2016 Neurology Collaborators. 2019. Global, regional, and national burden of neurological disorders, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet. Neurology* 18, 5 (May 2019), 459—480. https://doi.org/10.1016/s1474-4422(18)30499-x

[13] Jeffrey M. Gelfand. 2014. Chapter 12 - Multiple sclerosis: diagnosis, differential diagnosis, and clinical presentation. In *Handbook of Clinical Neurology*, Douglas S. Goodin (Ed.). Multiple Sclerosis and Related Disorders, Vol. 122. Elsevier, Radarweg 29, PO Box 211, 1000 AE Amsterdam, Netherlands, 269–290. https://doi.org/10.1016/B978-0-444-52001-2.00011-X

[14] Asavari S. Gowda, Areeba N. Memon, Erjola Bidika, Marina Salib, Bhavana Rallabhandi, and Hafsa Fayyaz. 2021. Investigating the Viability of Motor Imagery as a Physical Rehabilitation Treatment for Patients With Stroke-Induced Motor Cortical Damage. *Cureus* 13, 3 (March 2021), 1–14. https://doi.org/10.7759/cureus.14001 Publisher: Cureus.

[15] Siti Hazyanti Mohd Hashim, Marina Ismail, Haidzir Manaf, and Fazah Akhtar Hanapiah. 2019. Development of Dual Cognitive Task Virtual Reality Game Addressing Stroke Rehabilitation. In *Proceedings of the 2019 3rd International Conference on Virtual and Augmented Reality Simulations* (Perth, WN, Australia) *(ICVARS '19)*. Association for Computing Machinery, New York, NY, USA, 21–25. https://doi.org/10.1145/3332305.3332312

[16] Chien-Yu Huang, Wei-Chi Chiang, Ya-Chin Yeh, Shih-Chen Fan, Wan-Hsien Yang, Ho-Chang Kuo, and Ping-Chia Li. 2022. Effects of virtual reality-based motor control training on inflammation, oxidative stress, neuroplasticity and upper limb motor function in patients with chronic stroke: a randomized controlled trial. *BMC Neurology* 22, 1 (Jan. 2022), 21. https://doi.org/10.1186/s12883-021-02547-4

[17] Nancy Jacho-Guanoluisa, Sergio Albiol-Pérez, Cesar A. Collazos, Habib M. Fardoun, and Sandra Cano. 2019. Cognitive Rehabilitation Using Virtual Reality for Children with Rare Diseases. In *Proceedings of the 5th Workshop on ICTs for Improving Patients Rehabilitation Research Techniques* (Popayan, Columbia) *(REHAB '19)*. Association for Computing Machinery, New York, NY, USA, 183–186. https://doi.org/10.1145/3364138.3364176

[18] Ng Zhilong Jerome-Christian, B. S. Rajaratnam, and Tim Xu Tian. 2012. Can Virtual Reality Integrated within Conventional Rehabilitation Enhance Balance Recovery after Stroke?. In *Proceedings of the 6th International Conference on Rehabilitation Engineering & Assistive Technology* (Tampines, Singapore) *(i-CREATe '12)*. Singapore Therapeutic, Assistive & Rehabilitative Technologies (START) Centre, Midview City, SGP, Article 34, 4 pages.

[19] Hee-Tae Jung, Taiwoo Park, Narges MAhyar, Sungji Park, Taekyeong Ryu, Yangsoo Kim, and Sunghoon Ivan Lee. 2020. Rehabilitation Games in Real-World Clinical Settings: Practices, Challenges, and Opportunities. *ACM Trans. Comput.-Hum. Interact.* 27, 6, Article 41 (Nov. 2020), 43 pages. https://doi.org/10.1145/3418197

[20] Younbo Jung, Shih-Ching Yeh, and Jill Stewart. 2006. Tailoring Virtual Reality Technology for Stroke Rehabilitation: A Human Factors Design. In *CHI '06 Extended Abstracts on Human Factors in Computing Systems* (Montréal, Québec, Canada) *(CHI EA '06)*. Association for Computing Machinery, New York, NY, USA, 929–934. https://doi.org/10.1145/1125451.1125631

[21] Chethasi Kaluarachchi and Adel Al-Jumaily. 2011. Self-Rehabilitation Based on User Interactive Environment. In *Proceedings of the 5th International Conference on Rehabilitation Engineering & Assistive Technology* (Bangkok, Thailand) *(i-CREATe '11)*. Singapore Therapeutic, Assistive & Rehabilitative Technologies (START) Centre, Midview City, SGP, Article 52, 4 pages.

[22] Tamás Karácsony, John Paulin Hansen, Helle Klingenberg Iversen, and Sadasivan Puthusserypady. 2019. Brain Computer Interface for Neuro-Rehabilitation With Deep Learning Classification and Virtual Reality Feedback. In *Proceedings of the 10th Augmented Human International Conference 2019* (Reims, France) *(AH2019)*. Association for Computing Machinery, New York, NY, USA, Article 22, 8 pages. https://doi.org/10.1145/3311823.3311864

[23] Ilana Katz Sand. 2015. Classification, diagnosis, and differential diagnosis of multiple sclerosis. *Current opinion in neurology* 28, 3 (June 2015), 193—205. https://doi.org/10.1097/wco.0000000000000206

[24] M Kellor, J Frost, N Silberberg, I Iversen, and R Cummings. 1971. Hand strength and dexterity. *The American journal of occupational therapy : official publication of the American Occupational Therapy Association* 25, 2 (March 1971), 77—83. http://europepmc.org/abstract/MED/5551515

[25] Fary Khan, Bhasker Amatya, Mary P. Galea, Roman Gonzenbach, and Jürg Kesselring. 2017. Neurorehabilitation: applied neuroplasticity. *Journal of Neurology* 264, 3 (1 March 2017), 603–615. https://doi.org/10.1007/s00415-016-8307-9

[26] Ashley Knight, Stephanie Carey, and Rajiv Dubey. 2016. An Interim Analysis of the Use of Virtual Reality to Enhance Upper Limb Prosthetic Training and Rehabilitation. In *Proceedings of the 9th ACM International Conference on PErvasive Technologies Related to Assistive Environments* (Corfu, Island, Greece) *(PETRA '16)*. Association for Computing Machinery, New York, NY, USA, Article 65, 4 pages. https://doi.org/10.1145/2910674.2910717

[27] Gun A. Lee, Omprakash Rudhru, Hye Sun Park, Ho Won Kim, and Mark Billinghurst. 2017. User Interface Agents for Guiding Interaction with Augmented Virtual Mirrors. In *ICAT-EGVE 2017 - International Conference on Artificial Reality and Telexistence and Eurographics Symposium on Virtual Environments*, Robert W. Lindeman, Gerd Bruder, and Daisuke Iwai (Eds.). The Eurographics Association, Adelaide, Australia, 109–116. https://doi.org/10.2312/egve.20171347

[28] Rastislav Lipovský and Hugo Alexandre Ferreira. 2015. Self Hand-Rehabilitation System Based on Wearable Technology. In *Proceedings of the 3rd 2015 Workshop on ICTs for Improving Patients Rehabilitation Research Techniques* (Lisbon, Portugal) *(REHAB '15)*. ACM, New York, NY, USA, 93–95. https://doi.org/10.1145/2838944.2838967

[29] Jiazhen Liu and Joseph Finkelstein. 2018. Telerehabilitation System for Personalized Exercise Engagement of Patients with Multiple Sclerosis. In *2018 IEEE 31st International Symposium on Computer-Based Medical Systems (CBMS)* (Karlstad, Sweden). IEEE, Piscataway, New Jersey, United States, 446–447. https://doi.org/10.1109/CBMS.2018.00088

[30] J. A. Lozano-Quilis, H. Gil-Gómez, J. A. Gil-Gómez, S. Albiol-Pérez, G. Palacios, Habib M. Fardoum, and Abdulfattah S. Mashat. 2013. Virtual Reality System for Multiple Sclerosis Rehabilitation Using KINECT. In *Proceedings of the 7th International Conference on Pervasive Computing Technologies for Healthcare* (Venice, Italy) *(PervasiveHealth '13)*. ICST (Institute for Computer Sciences, Social-Informatics and Telecommunications Engineering), Brussels, BEL, 366–369. https://doi.org/10.4108/icst.pervasivehealth.2013.252208

[31] The-Kiet Lu, Edwin Foo, Bala S. Rajaratnam, and Kannappan. 2013. Configurable Augmented Virtual Reality Rehabilitation System for Upper Limb Disability. In *Proceedings of the 7th International Convention on Rehabilitation Engineering and Assistive Technology* (Gyeonggi-do, South Korea) *(i-CREATe '13)*. Singapore Therapeutic, Assistive & Rehabilitative Technologies (START) Centre, Midview City, SGP, Article 19, 4 pages.

[32] Maria Grazia Maggio, Margherita Russo, Marilena Foti Cuzzola, Massimo Destro, Gianluca La Rosa, Francesco Molonia, Placido Bramanti, Giuseppe Lombardo, Rosaria De Luca, and Rocco Salvatore Calabrò. 2019. VR in multiple sclerosis rehabilitation: A review on cognitive and motor outcomes. *Journal of Clinical Neuroscience* 65 (2019), 106–111. https://doi.org/10.1016/j.jocn.2019.03.017

[33] Thais Massetti, Isabela Lopes Trevizan, Claudia Arab, Francis Meire Favero, Denise Cardoso Ribeiro-Papa, and Carlos Bandeira de Mello Monteiro. 2016. Virtual reality in multiple sclerosis – A systematic review. *Multiple Sclerosis and Related Disorders* 8 (July 2016), 107–112. https://doi.org/10.1016/j.msard.2016.05.014 Publisher: Elsevier.

[34] Virgil Mathiowetz, Karen Weber, Nancy Kashman, and Gloria Volland. 1985. Adult Norms for the Nine Hole Peg Test of Finger Dexterity. *The Occupational Therapy Journal of Research* 5, 1 (1985), 24–38. https://doi.org/10.1177/153944928500500102 _eprint: https://doi.org/10.1177/153944928500500102.

[35] Motahare Mokhtarzade, Robert Motl, Raoof Negaresh, Philipp Zimmer, Mostafa Khodadoost, Julien S. Baker, Darpan Patel, Nastaran Majdinasab, and Rouholah Ranjbar. 2018. Exercise-induced changes in neurotrophic factors and markers of blood-brain barrier permeability are moderated by weight status in multiple sclerosis. *Neuropeptides* 70 (2018), 93–100. https://doi.org/10.1016/j.npep.2018.05.010

[36] R. Negaresh, R. W. Motl, P. Zimmer, M. Mokhtarzade, and J. S. Baker. 2019. Effects of exercise training on multiple sclerosis biomarkers of central nervous system and disease status: a systematic review of intervention studies. *European Journal of Neurology* 26, 5 (2019), 711–721. https://doi.org/10.1111/ene.13929

[37] Chris H Polman, Stephen C Reingold, Brenda Banwell, Michel Clanet, Jeffrey A Cohen, Massimo Filippi, Kazuo Fujihara, Eva Havrdova, Michael Hutchinson, Ludwig Kappos, Fred D Lublin, Xavier Montalban, Paul O'Connor, Magnhild Sandberg-Wollheim, Alan J Thompson, Emmanuelle Waubant, Brian Weinshenker, and Jerry S Wolinsky. 2011. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Annals of neurology* 69, 2 (Feb. 2011), 292–302. https://doi.org/10.1002/ana.22366 Publisher: Wiley Subscription Services, Inc., A Wiley Company.

[38] Wendy Powell, Vaughan Powell, and Maureen Simmonds. 2014. Virtual Reality for Gait Rehabilitation - Promises, Proofs and Preferences. In *Proceedings of the 7th International Conference on PErvasive Technologies Related to Assistive Environments* (Rhodes, Greece) *(PETRA '14)*. Association for Computing Machinery, New York, NY, USA, Article 16, 7 pages. https://doi.org/10.1145/2674396.2674450

[39] Magdalena Pruszyńska, Sławomir K. Tadeja, Marcin Świątczak, and Joanna Kostka. 2022. Zastosowanie interfejsów wirtualnych i innych cyfrowych technologii w rehabilitacji. *Med. Univ. of Lodz: UWM Medical Reports* 4 (April 2022), 1–46.

[40] Edgar Rodríguez Ramírez, Regan Petrie, Kah Chan, and Nada Signal. 2018. A Tangible Interface and Augmented Reality Game for Facilitating Sit-to-Stand Exercises for Stroke Rehabilitation. In *Proceedings of the 8th International Conference on the Internet of Things* (Santa Barbara, California, USA) *(IOT '18)*. Association for Computing Machinery, New York, NY, USA, Article 28, 4 pages. https://doi.org/10.1145/3277593.3277635

[41] Nathaniel Rossol, Irene Cheng, Walter F. Bischof, and Anup Basu. 2011. A Framework for Adaptive Training and Games in Virtual Reality Rehabilitation Environments. In *Proceedings of the 10th International Conference on Virtual Reality Continuum and Its Applications in Industry* (Hong Kong, China) *(VRCAI '11)*. Association for Computing Machinery, New York, NY, USA, 343–346. https://doi.org/10.1145/2087756.2087810

[42] Karl-Heinz Schulz, Stefan M. Gold, Jan Witte, Katharina Bartsch, Undine E. Lang, Rainer Hellweg, Rüdiger Reer, Klaus-Michael Braumann, and Christoph Heesen. 2004. Impact of aerobic training on immune-endocrine parameters, neurotrophic factors, quality of life and coordinative function in multiple sclerosis. *Journal of the Neurological Sciences* 225, 1 (2004), 11–18. https://doi.org/10.1016/j.jns.2004.06.009

[43] Y. Shen, S. K. Ong, and A. Y. C. Nee. 2008. An augmented reality system for hand movement rehabilitation. In *Proceedings of the 2nd International Convention on Rehabilitation Engineering & Assistive Technology (iCREATe '08)*. Singapore Therapeutic, Assistive & Rehabilitative Technologies (START) Centre, Midview City, SGP, 189–192.

[44] Y. Shen, S. K. Ong, and A. Y. C. Nee. 2009. Hand Rehabilitation Based on Augmented Reality. In *Proceedings of the 3rd International Convention on Rehabilitation Engineering & Assistive Technology* (Singapore) *(i-CREATe '09)*. Association for Computing Machinery, New York, NY, USA, Article 23, 4 pages. https://doi.org/10.1145/1592700.1592727

[45] Diana Siwiak, Nicole Lehrer, Michael Baran, Yinpeng Chen, Margaret Duff, Todd Ingalls, and Thanassis Rikakis. 2011. A Home-Based Adaptive Mixed Reality Rehabilitation System. In *Proceedings of the 19th ACM International Conference on Multimedia* (Scottsdale, Arizona, USA) *(MM '11)*. Association for Computing Machinery, New York, NY, USA, 785–786. https://doi.org/10.1145/2072298.2072456

[46] Richard H. Y. So, K. P. Wong, S. L. Yuen, J. Tang, H. Yeung, and J. Liu. 2011. Virtual Reality Gaming for Rehabilitation: An Evaluation Study with Physio- and Occupational Therapists. In *Proceedings of the 10th International Conference on Virtual Reality Continuum and Its Applications in Industry* (Hong Kong, China) *(VRCAI '11)*. Association for Computing Machinery, New York, NY, USA, 503–506. https://doi.org/10.1145/2087756.2087852

[47] Theo Theunissen, Carmen Ensink, René Bakker, and Noël Keijsers. 2020. Movin(g) Reality: Rehabilitation after a CVA with Augmented Reality. In *Proceedings of the European Conference on Pattern Languages of Programs 2020* (Virtual Event, Germany) *(EuroPLoP '20)*. Association for Computing Machinery, New York, NY, USA, Article 18, 7 pages. https://doi.org/10.1145/3424771.3424819

[48] Daria Tsoupikova, Yu Li, Nikolay Stoykov, Derek Kamper, and Randy Vick. 2009. Virtual Reality Environment Assisting Recovery from Stroke. In *ACM SIGGRAPH ASIA 2009 Sketches* (Yokohama, Japan) *(SIGGRAPH ASIA '09)*. Association for Computing Machinery, New York, NY, USA, Article 39, 1 pages. https://doi.org/10.1145/1667146.1667195

[49] João Vieira, Maurício Sousa, Artur Arsénio, and Joaquim Jorge. 2015. Augmented Reality for Rehabilitation Using Multimodal Feedback. In *Proceedings of the 3rd 2015 Workshop on ICTs for Improving Patients Rehabilitation Research Techniques* (Lisbon, Portugal) *(REHAB '15)*. Association for Computing Machinery, New York, NY, USA, 38–41. https://doi.org/10.1145/2838944.2838954

[50] Clare Walton, Rachel King, Lindsay Rechtman, Wendy Kaye, Emmanuelle Leray, Ruth Ann Marrie, Neil Robertson, Nicholas La Rocca, Bernard Uitdehaag, Ingrid van der Mei, Mitchell Wallin, Anne Helme, Ceri Angood Napier, Nick Rijke, and Peer Baneke. 2020. Rising prevalence of multiple sclerosis worldwide: Insights from the Atlas of MS, third edition. *Multiple sclerosis (Houndmills, Basingstoke, England)* 26, 14 (Dec. 2020), 1816–1821. https://doi.org/10.1177/1352458520970841 Edition: 2020/11/11 Publisher: SAGE Publications.

[51] Lynne M. Weber, Dawn M. Nilsen, Glen Gillen, Jin Yoon, and Joel Stein. 2019. Immersive Virtual Reality Mirror Therapy for Upper Limb Recovery After Stroke: A Pilot Study. *American Journal of Physical Medicine & Rehabilitation* 98, 9 (2019), 783–788. https://journals.lww.com/ajpmr/Fulltext/2019/09000/Immersive_Virtual_Reality_Mirror_Therapy_for_Upper.7.aspx

[52] Amy Webster, Matthieu Poyade, Scott Rooney, and Lorna Paul. 2021. Upper limb rehabilitation interventions using virtual reality for people with multiple sclerosis: A systematic review. *Multiple Sclerosis and Related Disorders* 47 (2021), 102610. https://doi.org/10.1016/j.msard.2020.102610

[53] Carla Winter, Florian Kern, Dominik Gall, Marc Erich Latoschik, Paul Pauli, and Ivo Käthner. 2021. Immersive virtual reality during gait rehabilitation increases walking speed and motivation: a usability evaluation with healthy participants and patients with multiple sclerosis and stroke. *Journal of NeuroEngineering and Rehabilitation* 18, 1 (April 2021), 68. https://doi.org/10.1186/s12984-021-00848-w
[54] Zhang Xiaoyu. 2010. Greatly Enhance National Control and International Competitive Power in the Field of Rehabilitation Technical Aids. In *Proceedings of the 4th International Convention on Rehabilitation Engineering & Assistive Technology* (Shanghai, China) *(iCREATe '10)*. Singapore Therapeutic, Assistive & Rehabilitative Technologies (START) Centre, Midview City, SGP, Article 68, 4 pages.