

Impact of Virtual Reality Program on Upper Limb Function Post Stroke: a randomized controlled trial

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ABSTRACT

Introduction: Motor function after stroke may be facilitated by the application of task-oriented approach which provides both functional and neurological recovery than otherwise possible. Also, virtual reality training promotes the restoration of movements by immersing the patient in an entertaining trial of performance.

Methods: To compare between the effect of virtual reality training program and task-oriented training program on the paretic upper limb function post stroke. Twenty subacute stroke survivors participated in the study. Participants were randomly allocated into one of two equal groups of 10; experimental group (A) and control group (B). Experimental group (A) performed a virtual reality program and task-oriented program, while Control group (B) performed task-oriented program only. Assessment was done for all participants using upper limb function index and grip strength test before (pre testing) and after six weeks of intervention (post testing).

Results: Paired *t*-test revealed that Virtual reality training group (Experimental group A) had statistical significant increases in the post testing mean values (after six weeks of intervention) of both upper limb functional index and hand grip strength compared to the pre testing values ($p < 0.05$). Furthermore, independent *t*-test showed a statistical significant increases in their post testing mean values in the experimental group A compared to the control group B.

Conclusion: The virtual reality training has a vital role in improving upper limb function and augmenting hand grip strength post stroke. It can be considered more effective than task-oriented in such cases.

Key words: virtual reality, upper limb, stroke, task oriented

Introduction

Stroke is a foremost reason for long-duration neurological disabilities in adults that results in difficulty to perform either self-care or community activities [1]. Loss of motor control of the upper limb is the greatest form of neurologic debility after brain stroke [2]. The paretic arm remains without function in between 32% to 34% of stroke survivors especially early after stroke according to the estimates of the cohort studies [3]. Return of voluntary arm motor control and function is an important goal during stroke rehabilitation to minimize the patient disability [4]. In spite of, most of recovery obtained in the first few weeks after stroke, patients may show functional improvements many months after having a stroke [5].

To achieve motor recovery after stroke, passive movement is not sufficient. Motor recovery depends on timing of intervention, repetition and intensity of exercises [6]. A concentrated training

related to specific goal is very beneficial for the development of independence and optimization of functional recovery [7]. The Task-oriented training was found to induce motor control and motor learning through practicing a group of selective meaningful functional tasks which made it easy to be transferred to real-life activities [8]. The Task-oriented training approach has a measurable effect on motor recovery of hand function and the whole paretic arm of stroke survivors. It can be explained with the neural plasticity induced by task-specific motor trainings and exercising [9] which was confirmed in functional neuroimaging studies [5, 10].

However, clinical trials suggested that the task-oriented training may be superior to other current clinical practices in upper extremity rehabilitation in stroke patients [11], Virtual Reality (VR) training is a such intervention that shows promise in stroke rehabilitation [12, 13]. The VR showed a great advancement in the application of healthcare because it provides patients with an immersive and entertaining approach that helps accomplish performance optimization [14]. The visual reality technology used in physical therapy helps the patients to re-learn the use of their upper limbs and return to normal limb function. This occurs through a motivating practice with a sufficient feedback for both the patient and the therapist about performance of the trained activity [15].

The Clinical application of VR in rehabilitation is a relatively novel, and its effectiveness is still questionable especially with the lack of randomized controlled studies and thus lack of the clinical evidence, especially early after stroke. Because of absence of a qualitative evidence for the superiority of the current practiced interventions for the upper limb motor training after stroke [5], there is a growing need to recognize the best training methods and protocols [16]. A number of training programs have been conducted to improve the upper limb functions. These have included VR training and the task oriented upper limb training [17]. Therefore, the aim of this study was to directly provide a clue to the preference of the application of VR-based training in comparison to the task oriented rehabilitation in improving upper limb function post stroke. The study was designed to investigate whether VR training as an adjunct to the task oriented training produces a significant improvement in the upper limb functional index and hand grip strength in the subacute phase after onset of stroke than the task oriented training alone. This study attempted to offer technologically entertaining exercises that were easy to be performed and were selected to emphasize the bilateral use of both the affected and the unaffected arm while going through the virtual training experience. This in turn provided both repetitive and entertaining upper limb rehabilitation to patients with subacute stroke focusing on improving paretic upper limb functions and increase muscle strength to obtain motor recovery [17].

Subjects and methods

Design of study

It is a pre-test post-test control group design. The study evaluates cause effect relationship between two groups; study group and control group at two times of testing; before and six weeks after interventions.

Participants

Twenty subacute stroke patient (less than 6 months after stroke) of both genders participated in the study. The patients' ages ranged from 55 to 65 years. All patients were diagnosed as CerebroVascular Accident (CVA) by specialized neurologist. All subjects were undergoing outpatient rehabilitation. Patients included in the study were visually intact with normal cognitive functions. This was easily confirmed since the patients were able to understand the physiotherapist's instructions and respond to the sections of testing appropriately. They also had mild spasticity according to Ashworth Scale (1, +1) [18]. However, patients who suffered from acute CVA with moderate to severe spasticity, impaired cognitive skills or any musculoskeletal deficit that affect their upper limb function were excluded from the study. Patients who met the inclusion criteria assigned an informed consent form upon agreement to participate in the study before participation in our clinical trial. Then, they were randomly subdivided into one of two

equal groups of 10; experimental group (A) performed VR and task oriented training programs and control group (B) only performed task oriented training program. Simple random allocation method was applied using statistical tables and both patients and examiners were blinded (double blinding randomization). Assessment of Upper Extremity Functional Index (UEFI) and grip strength for all patients in both groups were done twice; before and after six weeks of interventions. The study has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the Research Ethics Committee of Faculty of Rehabilitation Sciences, King Abdulaziz University, KSA. The decision number is FMRS-EC2020-02-004.

Assessment Tools

Upper Extremity Functional Index (UEFI) test

It is a reliable and valid test that assesses the performance of daily living activities using the upper limbs as household activities [19, 20]. It consists of 20-point area-specific and patient-described index. It examines the function of upper limb in individuals with hand and upper limb problems. Patients level the task on a 3:4 scale, as zero denotes maximum effort and four means no effort executing the task. This interprets into a maximum potential mark of 80, which denotes outstanding performance. UEFI requires nearby five minutes for completion and it is easy to be applied. Overall mark is calculated by additions of participants' marks.

Grip strength test

Hand held dynamometer is a valid and reliable device used to measure the grip strength through holding the handle with the patient hand, arm in adduction and elbow in 90° flexion resting on an arm chair or supported by the examiner hand²¹. The examiner asked the patient to squeeze as hard as possible then release. Based on the results, the strength increment could be measured. Many studies approved the validity and reliability of hand held dynamometer to measure grip strength.

Interventions

1. The VR training program

The VR training session lasted for 15 minutes and was done in a well-equipped room to give the patient the best VR training experience. The equipment included a screen to observe what the patient can see in the play as a feedback for the examiner, play station console, VR goggles to immerse the patient inside the game and controllers to play with.

At the beginning, the examiner taught the patient how to play by guiding the movement and then the patient was allowed to play alone. The game was called "SUPER PUNCH"; which is a boxing game with the patient sitting on a high back chair and with fistful hands holding twin packs in the starting position, the game allowed patients to bilaterally use their upper extremity with repetitive flexion-extension for elbow and shoulder to produce punching movements at different heights. The patient could reach by his/her hand in all directions "forward, upward, downward, left and right" to hit the paddles with boxing gloves. The game consists of three levels of playing; the highest level is above the head, the middle one is at 90° shoulder horizontal flexion and the lower one is 45°-35° shoulder flexion. During playing, the computerized system measures each punch at each level and gives the patients direct visual feedback via a five-written word from low to high performance (weak, slow, okay, good and perfect). This would enhance the eye- hand coordination and upper limb function. It's a timed game so the patient would be motivated each time he/she plays to get higher score. The time set for each games was two minutes and the game was repeated for five times per session with rest in between for 1–2 minutes. So, the total time of the VR training session was 10–15 minutes. It was done three times per week for six successive weeks.

2. The task-oriented training program

The program included 5–10 repetitions of selective motor training, selective functional movements and fine motor training. The selective motor training was in form of throwing activity of a standard volley ball that enabled gross upper extremity function and optical training program. The selective functional movements included reaching and manipulative tasks by using standard rehabilitation cones and washing pegs. Fine motor training involved a ball grip training by squeezing a ball of different shapes and sizes with thumb and fingers, playing with clay, holding a pin with thumb and index finger and practice of hand writing. The program was first done unilaterally then progressed to be done bilaterally. The total training session lasted for one hour and was applied 3 times per week for six successive weeks.

Statistical analysis

A pilot study was conducted before initiating the clinical part of the study with five participants to determine the appropriate sample size. Power analysis was calculated via power analysis equation at a significance level of 5% and a test power of 80%. The primary outcome measure was UEFI test value. Power analysis revealed that a minimum sample size of 20 participants were required for the study.

A total of 30 participants were assessed for eligibility to randomize patients' dropouts. Seven participants were excluded from the study because they did not meet the inclusion criteria and three participants declined to participate. Twenty participants were then randomized for allocation and subdivided into two groups: experimental group A ($n = 10$), control group B ($n = 10$) as presented in the Consort flow chart diagram (Figure 1).

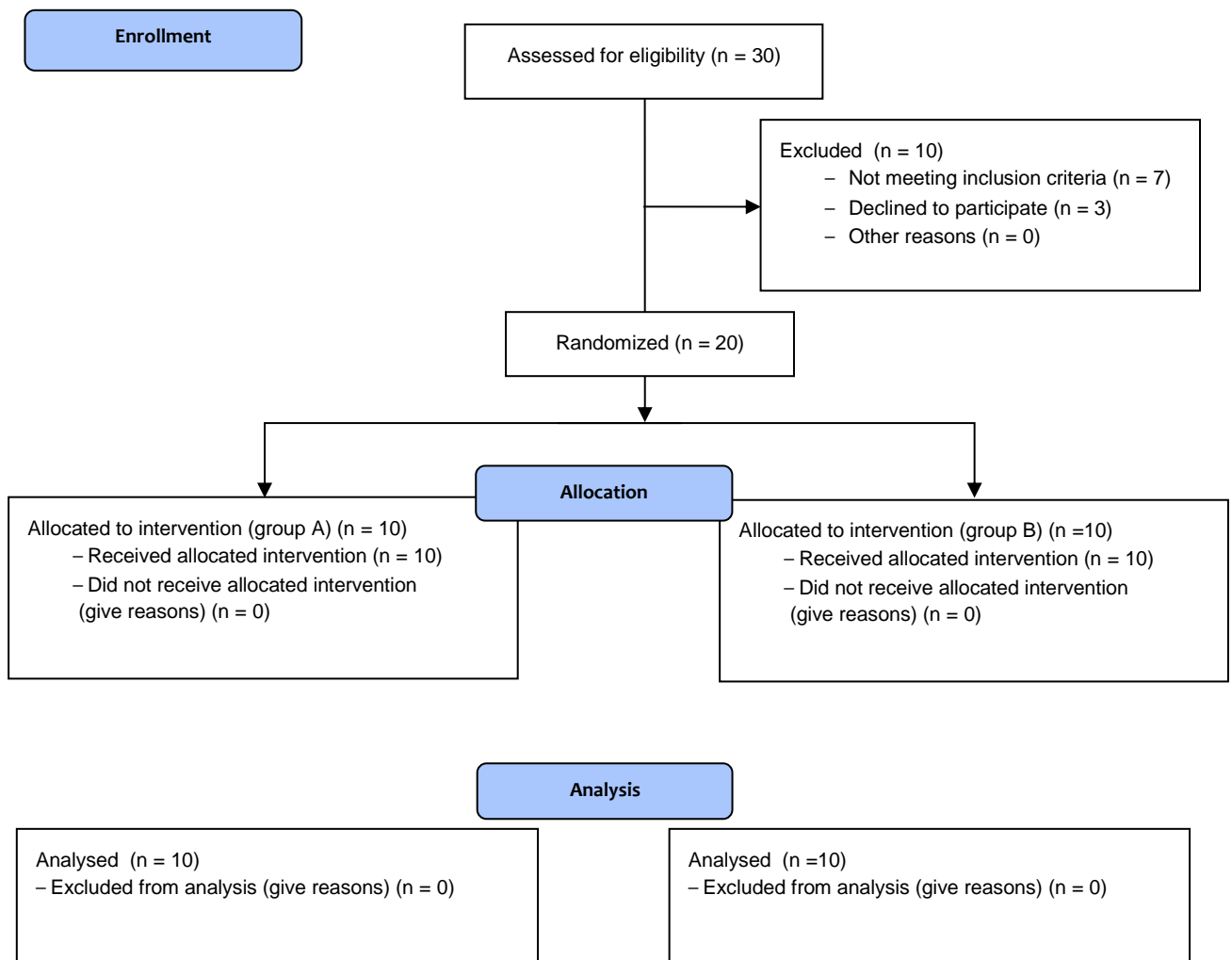


Figure 1. CONSORT 2010 Flow Diagram

Firstly, patient demographic data including age, body weight, and height were tested before initiating the study via independent *t*-test to assess homogeneity between the two groups. The mean values of age, body weight and height for the experimental group (A) were 54.20 ± 3.20 y, 88.20 ± 12.90 kg and 162.10 ± 5.40 cm, respectively. The mean values of age, body weight and height for the control group (B) were 56.40 ± 3.60 y, 79.20 ± 13.50 kg and 161 ± 7.60 cm, respectively. The independent *t*-test revealed no statistical significant differences between the two groups in all tested variables ($p > 0.05$) (Table 1).

Table 1. Patient demographic data

	Mean \pm SD		<i>t</i> - test	<i>p</i> -value
	Experimental group (A) <i>n</i> = 10	Control group (B) <i>n</i> = 10		
Age (y)	54.20 ± 3.20	56.4 ± 3.60	0.137	0.893
Body mass (kg)	88.20 ± 12.90	79.2 ± 13.50	-1.524	0.1448
Height (cm)	162.1 ± 5.40	161 ± 7.60	0.472	0.642

SD – standard deviation, level of significance at $p < 0.05$

After completing the study, data were collected and outcome measures were coded and studied by Microsoft Excel software. Data were then analysed through the Statistical Package for Social Sciences (SPSS) version 20 for Windows. Data exploration was done to assess for normality. Data were normally distributed with statistically insignificant Shapiro-Wilk test ($p > 0.05$) and normal frequency distribution curves, skewness and kurtosis. Paired *t*-test was then conducted to compare results within each group pre and post the intervention. Independent samples *t*-test was also used to compare the results between the two groups. Alpha level of significance was set at 0.05 for all the statistical tests.

Ethical approval

The study has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the Research Ethics Committee of Faculty of Rehabilitation Sciences, King Abdulaziz University, KSA (decision number: FMRS-EC2020-02-004).

Informed consent

Informed consent has been obtained from all individuals included in this study.

RESULTS

Statistical analysis using paired *t*-test demonstrated a statistical significant increase in the post test mean values of UEFI and grip strength compared with the pre-test mean values in the experimental group (A) ($p < 0.05$). In the control group (B), no statistical significant difference was detected between pre and post-test mean values of both UEFI and grip strength ($p > 0.05$). Independent *t*-test revealed no statistical significant differences in the pre-test mean values (baseline values) of UEFI and grip strength between both groups ($p > 0.05$). By comparing the post-test mean values between both groups, the results revealed a statistical significant increase in the UEFI and grip strength in the experimental group (A) compared with the control group (B) ($p < 0.05$) (Table 2, Figure 2, 3).

Table 2. Descriptive and inferential statistics of Upper Extremity Functional Index (UEFI) and grip strength pre and post intervention for both groups

Measured variables	Mean \pm SD			
	Experimental group (A)		Control group (B)	
	Pre-test	Post-test	Pre-test	Post-test
UEFI	42.50 \pm 15.70	55.10 \pm 12.90	41.1 \pm 11.50	50.4 \pm 13.47
Grip strength test	10.90 \pm 14.11	22 \pm 19.30	9 \pm 3.10	12 \pm 5.40
Statistical tests				
			<i>t</i> -test	<i>p</i> -value
Paired <i>t</i> -test (pre-test vs. post-test)	UEFI	Experimental group (A)	2.698	0.024
		Control group (B)	1.254	0.241
	Grip strength test	Experimental group (A)	3.757	0.005
		Control group (B)	1.50	0.241
Independent <i>t</i> -test [group (A) vs. group (B)]	UEFI	Pre-test	0.268	0.79
		Post-test	4.351	0.02
	Grip strength test	Pre-test	1.887	0.75
		Post-test	3.163	0.005

Level of significance at $p < 0.05$, SD – standard deviation

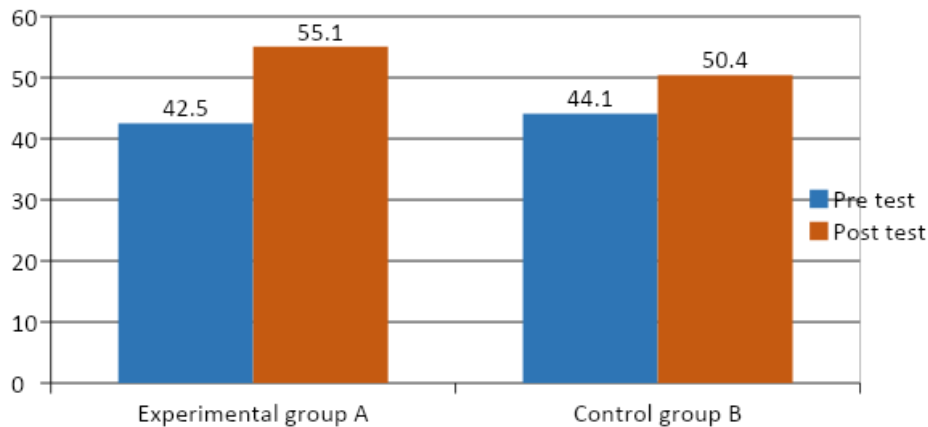


Figure 2. The mean values of Upper Extremity Functional Index (UEFI) pre and post treatment for both groups

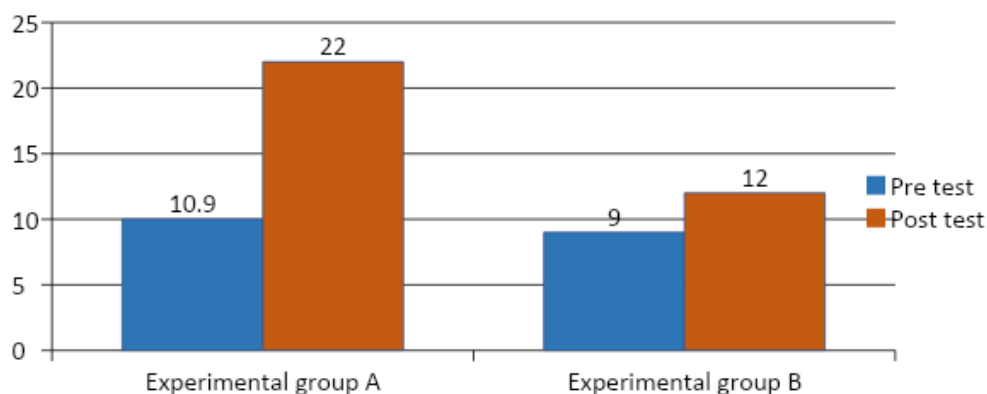


Figure 3. The mean values of grip strength pre and post treatment for both groups

Discussion

The outcomes of our study proved a statistical significant change in The UEFI and grip strength scores in the experimental group in comparison to the control group. This improvement in the experimental group more than the control group confirms the positive effect of this new technology in neurorehabilitation to potentiate motor recovery following stroke [22, 23]. It can be justified by practicing the upper limb movements in an enjoying experience with an instant

feedback either in visual or auditory form [24]. Moreover, it was done with constant motivation to complete the training session with high acceptability [25]. The repeated practice in such environment enhance the motor performance and induce neural plasticity [26] supported by the electroencephalogram (EEG) data especially in brain areas concerned with motor planning [27]. In addition, repetitive bilateral training using the controllers of the VR play from different levels and with motivation to hit the paddles strongly. The statistical significant improvement in the current study results can be also attributed to the positive effect of both symmetric and asymmetric bilateral activity of the upper limb movement while using the VR play which helps the patients to be interactive, highly responsive and motivated than performing the routine selected functional tasks of the prescribed task-oriented training program.

Although there was an increase in The UEFI and grip strength scores in the control group post testing, it was not statistically significant. This small variation may be due to the programmed repeated performances of meaningful and every day familiar tasks of the task-oriented training program. One critical element in functional recovery in the task-oriented training is the adaptation, which is achieved through focusing and active participation to achieve the functional tasks [28, 29].

The statistical significant improvement of the UEFI and grip strength scores in the experimental group more than the control group in the current study were in accordance to the work of Lee et al.³⁰ who examined eighteen stroke survivors to evaluate the influence of VR based bilateral upper limb physical activity on paralysed upper extremity function and muscular strength. Compared with the bilateral training group only concluded that the VR bilateral training program for six weeks improved the upper extremity function [31].

In the same context, Lee et al. [31] compared the effects of individualized VR program versus group-based rehabilitation program on upper extremity function and in certain daily living activities. They revealed a greater improvement in the The Fugl-Meyer Assessment (FMA) and Manual Function Test (MFT) in the VR group more than the group-based rehabilitation program.

However, the current study findings were in the opposite to the work of Kong et al. [32] who compared the efficacy of a commercial VR gaming device versus Nintendo wii and conventional therapy in facilitating upper extremity retrieval in 105 patients within six weeks post stroke. In addition, the current study results were opposed by the continuous three week study of Kong et al. [32] who indicated no difference in the scores of the Fugl- Myer Assessment (FMA) among the three studied groups. The results of Afsar et al. [33] study also opposed the current study results. They studied 35 stroke patients (19 VR group, 16 control group) before and after four weeks of intervention and concluded no difference between both studied groups in either the Functional independence measure gain nor the FMA gain [33].

However, the current study has some limitations including patient dropout, which was a reason for the decreased sample size. In addition, the selected VR training game (SUPER PUNCH) unfortunately emphasized only on the gross motor functions of the upper limb, so we couldn't train patients on the fine movements.

Conclusion

From our study findings, it can be concluded that the VR training program is more effective than the task-oriented training program in improving the upper extremity function after stroke.

Implications

Adding the VR training program to the physical therapy rehabilitation program of stroke patients helps them re-learn the use of their upper limbs and return to normal limb function.

The VR training program enhances faster recovery and gain of upper extremity function.

Recommendations

The authors recommend to increase the sample size for future studies investigating the effect of VR training program in such cases to be able to determine the effect size and generalize the results.

Additionally, we strongly recommended to use the VR training program in a home environment and in many other cases that seek motor control of upper extremity.

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Disclosure statement

No author has any financial interest or received any financial benefit from this research.

Conflict of interest

The authors state no conflict of interest.

References

1. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of stroke during 1990–2010: findings from the Global Burden of Disease Study. *Lancet Glob Health*. 2013;1(5):259–281; doi: 10.1016/S0140-6736(13)61953-4.
2. Au-Yeung SS, Hui-Chan CW. Predicting recovery of dextrous hand function in acute stroke. *Disabil Rehabil*. 2009;31(5):394–401; doi: 10.1080/09638280802061878.
3. Nijland RH, van Wegen EE, Harmeling-van der Wel BC, Kwakkel G. Presence of finger extension and shoulder abduction within 72 hours after stroke predicts functional recovery: early prediction of functional outcome after stroke: the EPOS cohort study. *Stroke*. 2010;41(4):745–750; doi: 10.1161/STROKEAHA.109.572065.
4. Coupar F, Pollock A, Van Wijck F, Morris J, Langhorne P. Simultaneous bilateral training for improving arm function after stroke. *Cochrane Database Syst Rev*. 2010;2010(4); doi: 10.1002/14651858.CD006432.pub2.
5. Pollock A, Farmer SE, Brady MC, Langhorne P, Mead GE, Mehrholz J, van Wijck F. Interventions for improving upper limb function after stroke. *Cochrane Database Syst Rev*. 2014;12(11):CD010820.
6. Holmgren E, Gosman-Hedström G, Lindström B, Wester P. What is the benefit of a high-intensive exercise program on health-related quality of life and depression after stroke? A randomized controlled trial. *Adv Physiother*. 2010;12(3):125–133; doi: 10.3109/14038196.2010.488272.
7. Langhammer B, Sunnerhagen KS, Lundgren-Nilsson Å, Sällström S, Becker F, Stanghelle JK. Factors enhancing Activities of Daily Living after stroke in specialized rehabilitation. An observational multicenter study within the Sunnaas International Network. *Eur J Phys Rehabil Med*. 2017;53(5):725–734. DOI:10.23736/S1973-9087.17. 04489-6.
8. Bosch J, O'Donnell MJ, Barreca S, Thabane L, Wishart L. Does task-oriented practice improve upper extremity motor recovery after stroke? A systematic review. *ISRN Stroke*. 2014.ges; doi: 10.1155/2014/504910.
9. Winstein CJ, Wolf SL, Dromerick AW, Lane CJ, Nelsen MA, Lewthwaite R, et al. Holley R. Interdisciplinary Comprehensive Arm Rehabilitation Evaluation (ICARE): a randomized controlled trial protocol. *BMC Neurol*. 2013;13(1):5; doi: 10.1155/2014/504910.
10. Beaulieu LD, Milot MH. Changes in transcranial magnetic stimulation outcome measures in response to upper-limb physical training in stroke: a systematic review of randomized controlled trials. *Ann Phys Rehabil Med*. 2018;61(4):224–234; doi: 10.1016/j.rehab.2017.04.003.

11. Thomas LH, French B, Coupe J, McMahon N, Connell L, Harrison J, et al. Repetitive task training for improving functional ability after stroke: a major update of a Cochrane review. *Stroke*. 2017;48(4):102–103; doi: 10.1161/STROKEAHA.117.016503.
12. Laver KE, Lange B, George S, Deutsch JE, Saposnik G, Crotty M. Virtual reality for stroke rehabilitation. *Stroke*. 2017;49(4):160–161; doi: 10.1002/14651858.CD008349.pub4.
13. Mazurek J, Kiper P, Cieřlik B, Rutkowski S, Mehlich K, Turolla A, Szczepańska-Gieracha J. Virtual reality in medicine: A brief overview and future research directions. *Human Movement*. 2019;20(3):16–22; doi: 10.5114/hm.2019.83529.
14. Fluet GG, Merians AS, Qiu Q, Rohafaza M, VanWingerden AM, Adamovich SV. Does training with traditionally presented and virtually simulated tasks elicit differing changes in object interaction kinematics in persons with upper extremity hemiparesis? *Top Stroke Rehabil*. 2015;22(3):176–184; doi: 10.1179/1074935714Z.0000000008.
15. Huang Q, Wu W, Chen X, Wu B, Wu L, Huang X, et al. Evaluating the effect and mechanism of upper limb motor function recovery induced by immersive virtual-reality-based rehabilitation for subacute stroke subjects: study protocol for a randomized controlled trial. *Trials*. 2019;20(1):104; doi: 10.1186/s13063-019-3177-y.
16. Hayward KS, Kramer SF, Thijs V, Ratcliffe J, Ward NS, Churilov L, et al. A systematic review protocol of timing, efficacy and cost effectiveness of upper limb therapy for motor recovery post-stroke. *Syst Rev*. 2019;8(1):187; doi: 10.1186/s13643-019-1093-6.
17. Kim WS, Cho S, Ku J, Kim Y, Lee K, Hwang HJ, Paik NJ. Clinical application of virtual reality for upper limb motor rehabilitation in stroke: review of technologies and clinical evidence. *J Clinic Med*. 2020;9(10):3369; doi: 10.3390/jcm9103369.
18. Ansari NN, Naghdi S, Arab TK, Jalaie S. The interrater and intrarater reliability of the Modified Ashworth Scale in the assessment of muscle spasticity: limb and muscle group effect. *NeuroRehabilitation*. 2008;23(3):231–237; doi: 10.3233/NRE-2008-23304.
19. Chesworth BM, Hamilton CB, Walton DM, Benoit M, Blake TA, Bredy H, et al. Reliability and validity of two versions of the upper extremity functional index. *Physiotherapy Can*. 2014;66(3):243–253; doi: 10.3138/ptc.2013-45.
20. Binkley JM, Stratford P, Kirkpatrick S, Farley CR, Okoli J, Gabram S. *Clin Breast Cancer*. 2018;18(6):1261–1267; doi: 10.1016/j.clbc.2018.02.008.
21. Amaral JF, Mancini M, Júnior JMN. Comparison of three hand dynamometers in relation to the accuracy and precision of the measurements. *Rev Bras Fisioter*. 2012;16(3):216–24.
22. Perez-Marcos D, Chevalley O, Schmidlin T, Garipelli G, Serino A, Vuadens P, et al. Increasing upper limb training intensity in chronic stroke using embodied virtual reality: a pilot study. *J Neuroeng Rehabil*. 2017;14(1):119; doi: 10.1186/s12984-017-0328-9.
23. Ahn S, Hwang S. Virtual rehabilitation of upper extremity function and independence for stroke: a meta-analysis. *J Exerc Rehabil*. 2019;15(3):358–369; doi: 10.12965/jer.1938174.087.
24. Aminov A, Rogers J M, Middleton S, Caeyenberghs K, Wilson P H. What do randomized controlled trials say about virtual rehabilitation in stroke? A systematic literature review and meta-analysis of upper-limb and cognitive outcomes. *J Neuroeng Rehabil*. 2018;27;15(1): 29; doi: 10.1186/s12984-018-0370-2.
25. Bergmann J, Krewer C, Bauer P, Koenig A, Riener R, Müller F. Virtual reality to augment robot-assisted gait training in non-ambulatory patients with a subacute stroke: a pilot randomized controlled trial. *Eur J Phys Rehabil Med*. 2018;54(3):397–407; doi: 10.23736/s1973-9087.17.04735-9.
26. Kossut M. Basic mechanism of neuroplasticity [in Polish]. *Neuropsychiatry Neuropsychology*. 2019;14(1):1–8; doi: 10.5114/nan.2019.87727.
27. Calabrò RS, Naro A, Russo M, Leo A, De Luca R, Balletta T, Bramanti P. The role of virtual reality in improving motor performance as revealed by EEG: a randomized clinical trial. *J Neuroeng Rehabil*. 2017;14(1):53; doi: 10.1186/s12984-017-0268-4.
28. Thant AA, Wanpen S, Nualnetr N, Puntumetakul R, Chatchawan U, Hla KM, Khin MT. Effects of task-oriented training on upper extremity functional performance in patients with sub-acute stroke: a randomized controlled trial. *J Phys Ther Sci*. 2019;31(1):82–87; doi: 10.1589/jpts.31.82.

29. Athanasiadis D, Protopsaltis S, Stefas E. The effects of Mobilization and Stimulation of Neuromuscular Tissue on the hemiplegic upper limb: a case report. *Physiother Quart.* 2019;27(1):6–11; doi: 10.5114/pq.2019.83055.
30. Lee S, Kim Y, Lee BH. Effect of virtual reality-based bilateral upper extremity training on upper extremity function after stroke: a randomized controlled clinical trial. *Occup Ther Int.* 2016;23(4):357–368; doi: 10.1002/oti.1437.
31. Lee M, Son J, Kim J, Pyun SB, Eun SD, Yoon B. Comparison of individualized virtual reality- and group-based rehabilitation in older adults with chronic stroke in community settings: a pilot randomized controlled trial. *Eur J Integr Med.* 2016;8(5):738–746; doi: 10.1016/j.eujim.2016.08.166.
32. Kong KH, Loh YJ, Thia E, Chai A, Ng CY, Soh YM, et al. Efficacy of a virtual reality commercial gaming device in upper limb recovery after stroke: a randomized, controlled study. *Top Stroke Rehabil.* 2016;23(5):333–340; doi: 10.1080/10749357.2016.1139796.
33. Afsar SI, Mirzayev I, Yemisci OU, Saracgil SNC. Virtual reality in upper extremity rehabilitation of stroke patients: a randomized controlled trial. *J Stroke Cerebrovasc Dis.* 2018;27(12):3473–3478; doi: 10.1016/j.jstrokecerebrovasdis.2018.08.007.