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Charlotte BERARD*

Manon CAVALIER**

Nathalie GODART***

Use of virtual reality-based therapy in the field of chronic stroke rehabilitation to improve hand function: asystematic review

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Wykorzystanie wirtualnej rzeczywistości w rehabilitacji dłoni u pacjentów po udarze mózgu: systematyczny przegląd literatury

Streszczenie

Udar mózgu jako schorzenie neurologiczne powoduje konieczność wielowymiarowego postępowania medycznego i fizjoterapeutycznego. Wirtualna rzeczywistość (VR) wydaje się być obiecującą technologią wsparcia rehabilitacyjnego, głównie poprzez możliwość odtworzenia rzeczywistych scenariuszy w środowisku generowanym komputerowo. VR może być uzupełnieniem kon-

* MSc student, Physiotherapy Department, International University of Health, Exercise & Sports, Differdange, Luxembourg; e-mail: berard.charlotte@stud.lunex-university.net

** MSc student, Physiotherapy Department, International University of Health, Exercise & Sports, Differdange, Luxembourg; e-mail: cavalier.manon@stud.lunex-university.net

*** MSc student, Physiotherapy Department, International University of Health, Exercise & Sports, Differdange, Luxembourg; e-mail: godart.nathalie@stud.lunex-university.net (corresponding author)

wencjonalnych metod rehabilitacji, poprawiając funkcje motoryczne dłoni oraz czynności dnia codziennego (ADLs). Celem niniejszego artykułu była ocena skuteczności terapii opartej na VR w celu poprawy funkcji dłoni u pacjentów po udarze mózgu. Artykuł został zaprojektowany jako systematyczny przegląd literatury. Przegląd literatury przeprowadzono przy użyciu baz bibliograficznych PubMed, Cochrane, Physiotherapy Evidence Database (PEDro) oraz rejestrów International Clinical Trials Registry Platform (ICTRP) i ClinicalTrials.gov., skąd finalnie wybrano 8 artykułów. Do przeglądu włączono randomizowane próby kliniczne (RCT), które dotyczyły interwencji VR w rehabilitacji funkcji dłoni u pacjentów po udarze mózgu. Podsumowując uzyskane wyniki, VR stosowana w rehabilitacji pacjentów po udarze mózgu poprawia funkcję dłoni i może być traktowana jako uzupełnienie do klasycznej rehabilitacji. Siedem z ośmiu włączonych badań uzyskało wysoki wynik w skali jakości PEDro. W przyszłych badaniach warto zwrócić uwagę na długotrwałe efekty rehabilitacji z wykorzystaniem VR.

Słowa kluczowe: wirtualna rzeczywistość, robotyka, VRET, dłoń, ręka, fizjoterapia, udar.

Abstract

A stroke is neurological damage that results in the need for medical and physical therapy management. From this perspective, virtual reality (VR) is a promising rehabilitation technology that reproduces real-life scenarios through computer-generated environments. VR can be a complementary strategy to conventional rehabilitation approaches by potentially improving hand motor function and activities of daily living (ADLs). This study aimed to evaluate the effectiveness of VR-based therapy in improving hand function for people suffering from chronic stroke. For this systematic review, we searched PubMed, Cochrane, Physiotherapy Evidence Database (PEDro) and registers on International Clinical Trials Registry Platform (ICTRP) and ClinicalTrials.gov including all eligible articles. In the end, 8 articles were included. Three reviewers independently searched for randomized controlled trials (RCT) of VR intervention in patients with chronic stroke, including only studies where hand function rehabilitation was specifically targeted. In conclusion, VR used in rehabilitation for patients with chronic stroke improves several outcomes of hand function and may be considered as an addition to rehabilitation in routine use. Seven out of eight included studies had a high-quality score on PEDro scale. Future studies should focus on how the advantages of VR therapy for hand function can be sustained over a longer period.

Keywords: virtual reality, robotics, VRET, hand, arm, physiotherapy, stroke.

Introduction

Stroke is an acute event that primarily involves neurological damage that leads to disability and mortality [11]. It is spread worldwide, with the consequence of being the second or third most common cause of death along with one of the leading causes of acquired adult disability [36]. Most recovery is considered achievable within the first few weeks of the initial illness, and moreover, long-term functional consequences can improve many months after the stroke [36]. A significant proportion of stroke-related disability includes sensory, cognitive and motor impairments, as well as reduced ability to perform activities of daily living (ADLs), decreasing social and community participation [30]. Limited

hand and arm functions have a significant repercussion on disability [21]. Training that is meaningful, consistently challenging, and highly repetitious is the best approach to regaining upper limb function [12, 20, 38].

VR is a high-tech computer-human interface system using hardware and software. It creates a multisensory stimulating environment through three-dimensional support and provides real-life scenarios with ADLs [19]. It proposes enhanced feedback through stimulation of the visual, vestibular, and somatosensory systems via virtual environment interaction [40]. The key aspect of VR is based on immersion and presence. There are 4 types of virtual degrees of immersion: non-immersive, immersive, augmented, and mixed VR. Presence is the subjective sensation of participants to which extent they perceive being in the virtual world, it depends on the degree of immersion, itself related to the virtual system [1, 19, 32].

This technological advance can be applied in the clinical or home setting [5, 35, 41]. However, VR is not yet widely used in rehabilitation even if it is becoming more affordable and cost-effective. Clinicians and researchers turned to other low-cost system options similar to interactive commercial video games which became more popular for VR-based therapy [27, 34]. This type of system is being adapted or designed for rehabilitation [24]. Compared to conventional therapy, VR may allow a patient to perform a higher dose of repetitious functional tasks [8]. Applying different VR systems to a stroke patient demonstrates certain benefits for the rehabilitation of upper and lower limb motor function [10, 18, 28, 29]. Additionally, adherence to treatment and motivation is increased with the use of VR, as it is considered more of a fun game rather than treatment, and not only in the field of stroke rehabilitation [28].

In the near future, new technology such as VR will be more implemented in clinical rehabilitation settings [4, 17, 33]. Therefore, it is important to assess the effectiveness of VR for specific types of patients to better adjust and guide future use and practice.

Recently, numerous systematic reviews have been evaluating the effectiveness of virtual reality for upper limb stroke rehabilitation, especially with commercial games [9, 25, 26]. The sufficiently encouraging results of the current studies animate the deepening of research on this subject.

The objective of this systematic review was to summarize the latest evidence concerning the effectiveness of VR-based therapy for the rehabilitation of hand function in stroke patients with chronic hemiparesis in comparison with hand rehabilitation, for instance, in the form of physiotherapy or occupational therapy. Our research question was as follows: In chronic stroke patients, what are the effects of VR treatment in comparison to hand functional therapy training to improve hand function?

Methods

Search strategy and study selection

The electronic search was performed on Physiotherapy Evidence Database (PEDro), PubMed, and Cochrane databases. In a similar manner, on ClinicalTrials.gov and the International Clinical Trials Registry Platform (ICTRP) to include studies that would conform to our criteria but would not be published yet. The search was run on 20 February 2020.

The search terms ‘hand’, ‘virtual reality’, ‘chronic’, ‘stroke’, and ‘physical therapy specialty’ were used for the advanced PubMed search, along with mesh terms and Boolean operators such as ‘AND’ between key terms and ‘OR’ between synonyms. Our search was adapted for different databases (Appendices 1–5). Three reviewers independently screened each record (title and abstract) from all databases according to predetermined eligibility criteria. Then the same reviewers screened all included trials for eligibility in the full text. All disagreements were resolved through discussion. The reviewers built in advance a table to report the wanted data (details in the ‘Data items’ section). The selected studies were divided between the reviewers and processed independently. No other instructions were put in advance except for the table, no training sessions likewise. All disagreements were resolved through discussion. All included articles were methodologically evaluated for risk of bias using the PEDro scale [39] by the same reviewer who collected the data.

In each study we sought the following information: study name, authors, and study type; number of participants per group; EG and CG training: duration and frequency of training, content of training such as tasks, exercises, and games used.; VR type; VR / robotic system: name and equipment used for the VR intervention; OM, assessment and corresponding results; the authors’ conclusions; grade on PEDro scale. All OM results included in our inclusion criteria were reported in Table 3 with their *P-value*.

Eligibility criteria

Regarding the chosen population, the chronic stage was announced after at least six months following the stroke [3], also with a clear presence of hemiparesis. We did not establish restrictions with respect to age, gender, duration of chronicity, severity of hemiparesis, and comorbidities. As minimal movements are required to perform VR training, patients with hemiplegia were excluded.

Only RCTs that evaluated the effects of training on the hand function were included. We define the hand as ‘five metacarpal bones, phalangeal bones, surrounding tissues, but anatomically the bones and tissues of the wrist are excluded’. RCT should present at least one comparison between a group using

VR-based treatment and another without VR. We did not set restrictions with regards to immersive type, exergaming was also accepted. Selected trials compared VR with conventional rehabilitation which is an umbrella term for all treatments used to regain motor function during the chronic stage after a stroke. For instance, we consider physiotherapy, occupational therapy, strengthening, and reaching tasks. The duration of both treatments and follow-up was not in scope.

The authors had to perform their assessment with at least one of the following outcome measures (OM) that include assessment of hand function: Fugl Meyer Assessment Scale (FMA), where hand subdivision should be separately reported from the rest of the limb evaluation, Wolf Motor Function Test (WMFT), Action Research Arm Test (ARAT), Jebsen Hand Function Test (JHFT) and Box and Block Test (BBT). If our population of interest was mixed with another, separate results should be provided. We filter using two assumptions that we made. If hand training was not explicit, we considered that it was not trained. However, we accepted the use of remote control in the VR program as hand rehabilitation. Finally, we did not discriminate results as far as publication dates were concerned. We excluded studies that were not available entirely in English or French.

Results

Study selection

Through the different databases and registers, we identified, after removing duplicates, 128 articles. Then, after reading each title and abstract, we excluded 87 articles as they did not comply with our eligibility criteria. During our search, 18 studies were eliminated because they were not entirely available or not in English or French. Following this, all 3 reviewers read the 23 articles in full text and 8 of them were finally included in our research with regard to our data item criteria. A PRISMA flow diagram [31] was created (Figure 1).

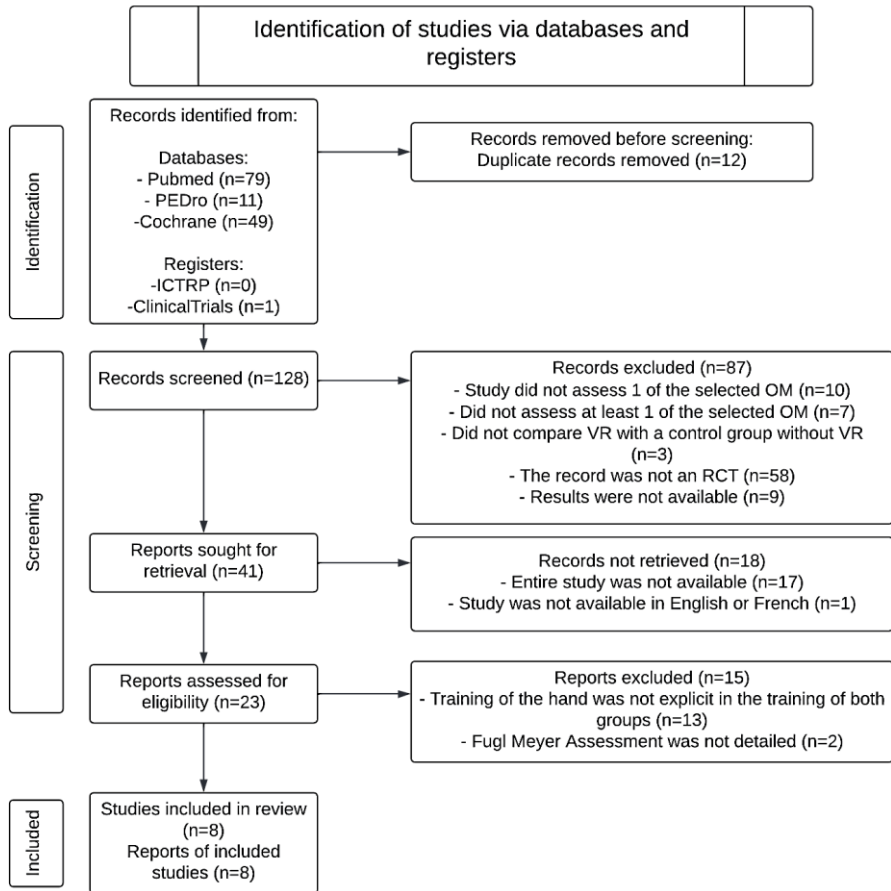


Figure 1. PRISMA flow diagram

Study characteristics

Table 1. Characteristics of the included studies

Authors (year) (1)	Group characteristics (number of participants) (2)	Control group training (3)	Experimental group training (4)	VR type (5)	VR system/robotic system (6)	Outcome measure and assessment (7)	Conclusion (8)
Huang et al., (2022)	<p>Chronic stroke</p> <p>CG (15): conventional occupational therapy</p> <p>EG (15): Immersive VR-based motor control training</p>	<p>16 sessions of intervention for 60 min/day, 2 to 3 days/week</p> <p>Supervised by an occupational therapist</p> <p>6–10 tasks at each session such as the peg board, climbing ladder and stacking cones</p>	<p>16 sessions of intervention for 60 min/day, 2 to 3 days/week</p> <p>6–10 tasks of VR scenes: Selected scenes were chosen based on the original upper limb activities (bilateral arm, one hand, aiming, shooting, hitting, waving arms, punching, and throwing object, shopping, pouring water, and blending drinks).</p> <p>20 different scenes</p>	Immersive VR	<p>Commercial immersive VR headset developed by HTC VIVE (HTC Corporation, New Taipei City, Taiwan).</p> <p>HMD device</p> <p>2 controllers</p> <p>2 infrared laser emitter units</p>	<ul style="list-style-type: none"> – FMA-UE – AROM – Simulator Sickness Questionnaire – Borg Scale of Perceived Exertion – Serum sampling for molecular biomarkers <p>Assessment: within one week before and after interventions</p>	<p>FMA-UE-Total score, and AROM-Shoulder Flexion was significantly higher in the EG than in the CG</p>

Table 1. Characteristics of the included studies (cont.)

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Ain et al., (2021)	<p>CG (25): exercise training group</p> <p>EG (25): Xbox Kinect training group + CT</p>	<p>Session with trained physiotherapist 35–40 min, 5 days/week for 6 weeks:</p> <ul style="list-style-type: none"> – Stretching (mild to moderate sustained in free pain range) (10–30 sec) – Weight bearing position in upper limb extension (1-3 times) – Exercises: tasks related to activities of daily living, such as lifting baskets, folding towels, turning a key in the lock, reaching forward, reaching sideways, grasping the ball, picking up small blocks and lifting cans and pencils (each task 3–4 min) 	<p>Intervention of 35-40 min, 5 days/week for 6 weeks. Intervention supervised by a physical therapist. Each session with conventional training exercises for 20 min.</p> <ul style="list-style-type: none"> – First week: orientation week (Patients' training for intervention + demonstration – 2nd & 3rd weeks: game named "tennis player," – 3rd & 4th weeks: "tennis player" + "joy riding" game – 5th & 6th weeks: 'tennis player' + "joy riding" + "Rally ball" <p>All games performed in a standing position</p>	Gaming	<p>Xbox Kinect 360: Kinect adventure pack & Kinect sports pack = upper extremity movement games</p> <p>LED screen for virtual environment</p>	<ul style="list-style-type: none"> – FMA-UE – BBT – Montreal Cognitive Assessment <p>Assessment: baseline and after completion of the intervention in the sixth week</p>	<p>EG: promising potential to enhance upper limb motor function for stroke patients</p>

Table 1. Characteristics of the included studies (cont.)

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
El-Kafy et al., (2021)	<p>Chronic stroke (6–24 months)</p> <p>CG (19): 2 h functional training</p> <p>EG (18): 1 h functional training + 1 h VR</p>	<p>Personalized face-to-face session (3 sessions of 2 h per week for 3 months)</p> <p>1st part (1 h):</p> <ul style="list-style-type: none"> – Muscle facilitation exercises – Proprioceptive neuromuscular facilitation exercises – Strengthening Activities – Stretching exercises – Postural reactions exercises <p>2nd part (1 h):</p> <ul style="list-style-type: none"> – Arm reaching tasks – Arm-hand tasks – Manipulative tasks (grasping and release activities) – ADLs task with both arms 	<p>Personalized face-to-face session (3 sessions of 2 h per week for 3 months)</p> <p>First and second part of functional training = 1 h</p> <p>3rd part for (1 h):</p> <ul style="list-style-type: none"> – VR-based training program using games (Armeo Spring): To simulate a range of upper limb – Arm-reaching + grasp (arm-hand activities) – Manipulative tasks 	<p>Single arm exoskeleton + hand training in an extensive 3D workspace</p>	<p>Armeo Spring equipment (MRF; Hocoma, Switzerland)</p> <p>It includes adjustable arm support (augmented feedback) and large 3D workspace</p>	<ul style="list-style-type: none"> – ARAT – WMFT – WMFT-Time (time required to complete the test) – Hand Grip Strength <p>Assessment: baseline and after completion of the treatment</p>	<p>Combined treatment of VR + CT is more effective in improving upper limb functions in individuals with chronic stroke than CT alone</p>

Table 1. Characteristics of the included studies (cont.)

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Marques-Sule et al., (2021)	CG (14): CT EG (15): VR with Nintendo Wii + CT	2 sessions of 2 hours per week, 4-week duration Protocol: <ul style="list-style-type: none"> - Warm-up - Mobility and strengthening exercises in supine position - Active-assisted/passive lower and upper limb kinesiotherapy - Upper-limb strengthening exercises using weights and elastic bands - Balance, stability, and coordination exercises - Walking exercises - Cool-down 	Same as CT + 2 sessions (30 min) per week of VR-Wii <ul style="list-style-type: none"> - Wii Fit package for balance training (lower limb): heading, ski slalom, tilt table, tightrope tension, downstream, subzero fishing - Wii Sports package (upper limb): bowling, golf, and tennis games Each game was performed as 2 sets with a 1-minute rest interval between each game	Gaming	Nintendo Wii (Nintendo, Kyoto, Japan) <ul style="list-style-type: none"> - Wii Remote: wireless controller - Wii Balance Board: lightweight board 	<ul style="list-style-type: none"> - FMA-UE - Timed Up and Go - Tinetti test - Performance-Oriented Mobility Assessment - Berg Balance Scale - Barthel Index - Frenchay Activity Index Assessment: at baseline and at the end of the study.	Promising results in functionality, balance, and ADLs when adding VR with Nintendo Wii to CT in chronic stroke survivors

Table 1. Characteristics of the included studies (cont.)

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Hung et al., (2019)	<p>CG (16): upper limb therapist-based training</p> <p>EG (17): Kinect2Scratch games</p>	<p>2–3 sessions / week, total of 24 sessions (3 months)</p> <p>15 min: ADLs training</p> <p>30 min: conventional hand function training Individual face-to-face session with trained occupational therapist</p> <p>30 min:</p> <ul style="list-style-type: none"> – Bimanual and unimanual exercises – Single and multiple joint training (shoulder, elbow and forearm) – Exercises personalized for each patient. <p>Verbal feedback and manual correction were allowed</p> <p>Each session included 3–4 movement patterns</p>	<p>2–3 sessions / week, total of 24 sessions (3 months)</p> <p>15 min: ADLs training</p> <p>30 min: conventional hand function training</p> <p>30 min:</p> <p>Each session: 3–4/8 games (Whack-a-mole, harvest carrots, picking apples, bowling, alien attack, hungry shark, hungry ant, boxing)</p>	Gaming	<p>Kinect2Scratch support with games</p> <p>Microsoft Kinect controller</p> <p>Alarm system: compensatory movement</p>	<ul style="list-style-type: none"> – FMA-UE: (Proximal: Shoulder, elbow, and forearm; Distal: wrist and hand) – WMFT (time + functional ability) – Motor Activity Log – Pittsburgh Participation Scale <p>Evaluation: at baseline, after intervention and 3 months after follow-up</p>	<p>VR as effective as CT, but could decrease the workload of therapists</p>

Table 1. Characteristics of the included studies (cont.)

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Kottink et al. (2014)	CG (10): conventional reaching tasks EG (8): Rehab game	30 min/3 days/6 weeks with trained therapist Neurorehabilitation approach: <ul style="list-style-type: none"> – Reaching a target positioned on a table – Mechanical exercises (e.g. bow, peg in holes, placing disks) Level of difficulty adjusted to patients' capability	30 min/3 days/6 weeks with trained therapist Game: 'Furball Hunt' The patient had to slide their finger (reaching task) onto a horizontal screen to play the game. As quick as possible	Gaming	Horizontal screen Webcam	<ul style="list-style-type: none"> – ARAT – FMA-total – Intrinsic Motivation Inventory Questionnaire Assessment: 1 week before and 1 week after the training sessions + 1 month after follow-up	VR and CG make the same progress. Patient may be more independent in their rehab in VR
Thielbar et al., (2014)	Chronic stroke with moderate hand impairment CG (7): Occupational therapy EG (7): Actuated Virtual Keypad Training	1 h – 3x /week, during 6 weeks Occupational therapy session: <ul style="list-style-type: none"> – Fine motor control – Dexterity – In-hand manipulation – Finger individuation The levels of activities are adjusted to the abilities of the patient. Treatment exercises: buttoning, typing, tying knots, writing and using tools	1 h – 3x /week, during 6 weeks 2 modes: 1st: <ul style="list-style-type: none"> – Patients press, hold, and release 1 or more keys as instructed on the screen – Visual and auditive feedback is provided. 2nd: <ul style="list-style-type: none"> – Song mode – Visual feedback + score The glove enables and prevents movements of the fingers (individually) by an air chamber system	Gaming	Actuated Virtual Keypad system PneuGlove (adjustable air pressure on the palmar surface & sensors at different hand joints) Software platform Virtools (Dassault Systemes, France) (represent 1 hand and 5 keys) Graphical user interface (physio-specific access)	<ul style="list-style-type: none"> – JTHFT – ARAT – FMA-UE + Hand subcomponent – Grip and pinch strengths Assessment: At baseline, after treatment and 1-month post-treatment	Only EG presented statistically significant improvement in measures of impairment (FMUE) and measures of task performance (JTHFT)

Table 1. Characteristics of the included studies (cont.)

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
In et al., (2012)	Chronic stroke CG (8): CT (sham program) EG (11): VR Reflection Therapy program	30 minutes a day, 5 days a week for 4 weeks The same settings as VR groups. But the screen is off, so patients look at their unaffected arm. Difficulty increases progressively (harder tasks are given): 1 st week: – Forearm, wrist, and grasp 2 nd week: – Gross motor functions (e.g. lifting a cup) 3 rd week: – Fine motor functions (e.g., pegging clothespins, pushing buttons on a calculator, using chopsticks, and opening a bottle). 4 th week: – Complicated tasks (e.g. puzzles, drawing a circle/square with a pen, toy golf) 3 sets of 10 repetitions	30 minutes a day, 5 days a week for 4 weeks VR Reflection Therapy program (Based on the principle of mirror therapy): – Placing the affected hand under a box (screen on the top) – The other (non-affected) hand placed under a camera to perform various hand movements which will be displayed on the screen. – 3 sets of 10 repetitions of movements.	VR	Laptop Camera Screen	– FMA-UE – Modified Ashworth Scale – BBT – JTHFT – Manual Function Test Assessment: pre- and post-intervention	Both groups increased their motor recovery and motor function in the upper extremities with a more significant improvement for the EG

EG: Experimental Group; VR: Virtual Reality; CG: Control Group; FMA-UE: Fugl Meyer Assessment-Upper Extremity; AROM: Active Range of Motion; CT: Conventional Therapy; BBT: Box and Block Test; ADLs: Activities of Daily Living; ARAT: Action Research Arm Test; WMFT: Wolf Motor Function Test; JTHFT: Jebsen-Taylor Hand Function Test.

Risk of bias assessment

The risk of bias of the 8 included articles was evaluated with the PEDro scale [39] to determine their quality, based on their internal validity and statistical information provided: 7 articles had a score between 6 and 10 which makes them high-quality studies, and 1 was marked 4, indicating fair quality. None of them had blinded therapists and only two articles had blinded assessors, while all had random allocation, baseline comparability, between-group comparisons, and point estimates and variability. Therefore, the overall quality was considered good. Each article assessment was reported in Table 2.

Table 2. Risk of bias assessment according to the PEDro scale

Studies	Huang et al. (2022)	Ain et al., (2021)	El-Kafy et al. (2021)	Hung et al. (2019)	In et al. (2012)	Kottink et al. (2014)	Marques-Sule et al. (2021)	Thielbar et al. (2014)
Eligibility criteria*	+	+	+	+	+	+	+	-
Random allocation	+	+	+	+	+	+	+	+
Concealed allocation	+	-	+	+	-	-	+	-
Baseline comparability	+	+	+	+	+	+	+	+
Blind subjects	+	-	-	-	-	-	+	-
Blind therapists	-	-	-	-	-	-	-	-
Blind assessors	+	+	+	+	-	+	+	+
Adequate follow-up	+	+	+	+	-	+	+	+
Intention-to-treat analysis	+	-	-	-	-	-	+	-
Between-group comparisons	+	+	+	+	+	+	+	+
Point estimates and variability	+	+	+	+	+	+	+	+
Total score	9/10	6/10	7/10	7/10	4/10	6/10	9/10	6/10

* This item is not counted in the total score; +: yes; -: no

Systematic analysis

The results showed that the EG always improved significantly when using WMFT, JHFT, and BBT. Some studies found that EG was significantly better than CG after interventions with ARAT, WMFT, BBT, and FMA. But that was not the

majority of the findings, except for ARAT. The results are shown in Table 3 [1, 10, 13–15, 22, 29, 37].

Table 3. Results of each outcome measure

Outcome measure	Studies	Results
ARAT (n = 69)	El-Kafy et al. (2021)	Between pre- and post-intervention: Significant improvement for both groups (<i>P</i> -value = 0.003, CG; 0.001, EG) EG improved significantly more than CG (<i>P</i> -value = 0.0034)
	Kottink et al. (2014)	Between pre- and post-intervention: Significant improvement for both groups (<i>P</i> -value <0.009) No significant differences between 2 groups (<i>P</i> -value ≥ 0.34)
	Thielbar et al. (2014)	Between pre-intervention and follow-up: No significant improvement in both groups. (<i>P</i> -value = 0.89, CG; 0.142, EG) Between pre- and post-intervention: EG was significantly better than CG (follow-up) (<i>P</i> -value = 0.022)
WMFT (n = 70)	El-Kafy et al. (2021)	Between pre- and post-intervention: Significant improvement for both groups Test component (<i>P</i> -value = 0.0031, CG; 0.001, EG) Time component (<i>P</i> -value = 0.0017, CG; 0.0001, EG) EG improved significantly more than CG Test component (<i>P</i> -value = 0.0015) Time component (<i>P</i> -value = 0.0014)
	Hung et al. (2019)	Between pre-intervention and follow-up: Significant improvement in time for both groups (<i>P</i> -value = 0.002, CG; 0.001, EG) Significant improvement for EG in the test feasibility but not in CG (<i>P</i> -value = 0.26, CG; 0.04, EG) No significant differences between 2 groups (<i>P</i> -value = 0.71, time; 0.63, feasibility)
JHFT (n = 33)	Thielbar et al. (2014)	Between pre-intervention and follow-up: No significant improvement for CG (<i>P</i> -value = 0.65) Significant improvement for EG (<i>P</i> -value = 0.02) Between pre- and post-intervention: No significant differences between both groups (<i>P</i> -value = 0.07)
	In et al. (2012)	Between pre and post-intervention: Significant improvement in EG (<i>P</i> -value ≤0.05) No significant difference between the groups

Table 3. Results of each outcome measure (cont.)

Outcome measure	Studies	Results
BBT (n = 119)	Ain et al. (2021)	Between pre and post-intervention: Significant improvement within the groups for both hands (P -value < 0.001) Significant difference between the groups for both hands (P -value < 0.001)
	In et al. (2012)	Between pre- and post-intervention: Significant improvement in EG (P -value \leq 0.05) No significant difference between the groups
FMA-UE(n = 206)	Huang et al. (2022)	Between the groups in the pre- and post-intervention intervention: No significant differences within and between the groups for hand
	Ain et al. (2021)	Between the groups in the pre- and post-intervention intervention: Significant improvement everywhere except in hand for CG – FMA-hand (P -value = 0.011, EG; 0.54, CG) – FMA-grasp (P -value < 0.001, EG; 0.01, CG) Significant difference between groups: – FMA-hand (P -value = 0.05) – FMA-grasp (P -value = 0.004)
	Marques-Sule et al. (2021)	Between pre- and post-intervention: No significant differences within and between the groups for hand
	Hung et al. (2019)	Between pre-intervention and follow-up: No significant improvement for both groups between pre-intervention and follow-up (include wrist and hand testing) (P -value = 0.08, CG; 0.10, EG) No significant differences between the groups (P -value = 958)
	Thielbar et al. (2014)	No significant improvement in both groups between baseline and follow-up (P -value = 0.58, CG; 0.34, EG)

EG: Experimental Group; CG: Control Group; FMA-UE: Fugl Meyer Assessment-Upper Extremity; BBT: Box and Block Test; ARAT: Action Research Arm Test; WMFT: Wolf Motor Function Test; JHFT: Jebsen-Taylor Hand Function Test.

Discussion and Conclusions

The purpose of this systematic review was to evaluate the effect of VR therapy on hand function in patients with chronic stroke. The articles were collected

and reported in a table to be easily investigated. We identified eight studies involving a total of 230 participants suffering from chronic stroke. VR therapy was compared to active control interventions. Our purpose was to analyze whether VR therapy caused greater improvements in hand function, especially in hand motor function, dexterity, coordination, strength, grasp, and activity limitations.

Only 5 of the studies included FMA with the hand subdivision reported, and only 1 study found significant improvements and differences between the VR groups. 2 studies included BBT (dexterity, coordination, and ADL), JHFT (ADLs), and WMFT (dexterity and strength), and they all found significant improvements in hand function when using VR therapy. Unfortunately, only one study for WMFT and one for BBT found significant differences between groups. Lastly, only 2 out of the 3 studies exploring ARAT (Grasp, ADL, dexterity, and coordination) found more improvement when using VR therapy compared to the control group. No strong evidence was found to confirm that VR-therapy benefits were sustained after the intervention. Only 3 studies completed a follow-up assessment, 1 after 3 months and 2 after 1 month. The only sustained improvements were found in 1 study for the WMFT after 3 months of intervention and for JHFT after 1 month of intervention. Therefore, most of the studies investigate short-term VR therapy with respect to hand function in patients with chronic stroke.

Although we focused our research on hand rehabilitation, the recovery of upper limb function using VR therapy in patients with chronic stroke is already well covered. For instance, a similar systematic review assessing upper limb recovery concluded that VR therapy was not superior to conventional therapy [2]. Even if superiority was not proven, there are systematic reviews that validate VR therapy use for chronic stroke rehabilitation [26]. However, there is a paucity of evidence on the effectiveness of VR therapy focusing on hand function. The latest systematic review and meta-analysis [6] observed significant subgroup differences in hand dexterity (BBT) and hand motor ability (WMFT and JHFT).

Some unknowns are important to consider for future research, such as the ideal duration of the treatment session and the optimal length of the program to obtain maximum benefits from VR-based treatment. In addition, more research is required on the long-term effect of VR training and the impact of a more immersive 3D experience on motor training. Future research would need a larger-scale RCT to facilitate the generalization of results. Furthermore, studies should implement treatment outcomes focusing on evaluating its relevant aspects such as adherence, satisfaction, or motivation to VR exercise. Along with the development of oriented games for rehabilitation rather than using commercial games.

Multiple advantages are reflected by the use of VR in clinical practice. First, it enables more independent training in an active and motivating way[16], by giving more control and autonomy to the patient over their rehabilitation. Ad-

ditionally, it could reduce therapists' workload and provide more accurate patient follow-ups. Moreover, it creates opportunities for home-based training and VR-enhanced feedback to promote motor learning in patients. Finally, VR equipment, such as commercial games, is a simple and inexpensive tool to add to rehabilitation. On the contrary, many innovative technologies in this field are usually complex, expensive, and only available in specialized centers, thus limiting their use.

This study has shown some limitations. First, the scarcity of studies analyzing certain outcomes, which could impact results and validity of our paper. VR has shown significant global effects on improving hand function, but it did not supersede other treatments. However, the literature supports the view that a combination of both therapies has a better effect than conventional treatments commonly used.

This systematic review indicates that VR has shown significant global effects on improving hand function but was not a better treatment than conventional ones. There are results that support VR over conventional treatment when combined with other physical therapy. A total of five outcomes were explored, and significant improvements were identified in 4 of them except for FMA. Only 3 out of 5 outcomes had significant differences between the groups, but this was not supported by all the studies exploring these outcomes. We have addressed the limitations of each paper through a comprehensive risk of bias assessment. As a result, 7 out of 8 articles were considered high quality, which supports the veracity of the results of this systematic review. In conclusion, VR used in rehabilitation for patients with chronic stroke improves several outcomes of hand function and may be considered an addition to routine rehabilitation. Future studies should focus on how the advantages of VR therapy for hand function can be sustained over a longer period of time.

Appendix

Appendix 1. PubMed search strategy

((("Hand"[MeSH Terms]) OR ("wrist"[MeSH Terms]) OR (finger) OR ("Hand Joints"[MeSH Terms]) OR ("Hand strength"[MeSH Terms]) OR (Box and block test) OR (BBT) OR (Purdue Pegboard Test) OR (PPT) OR (Fugl-Meyer Assessment Test) OR (FMA) OR (Wolf Motor Function Test) OR (WMFT) OR (grip) OR (pinch) OR (Action Research Arm Test) OR (ARAT) OR (Jebsen Hand Function Test) OR (JHFT) OR (hand strength rehabilitation[MeSH Terms])) AND ((virtual reality[Title/Abstract]) OR (VR[Title/Abstract]) OR (Simulated 3D environment[Title/Abstract]) OR (virtual reality exposure[Title/Abstract]) OR (virtual reality exposure therapy[Title/Abstract]) OR (virtual reality therapy[Title/Abstract]) OR ("virtual reality"[MeSH Terms]) OR ("virtual reality exposure therapy"[MeSH Terms])) AND (Chronic[title/abstract]) AND ((stroke[Title/Abstract]) OR (post-stroke[Title/Abstract])) AND (("Physical Therapy Specialty"[MeSH Terms]) OR ("Physical Therapy

Modalities" [MeSH Terms]) OR (physiotherapy[Title/Abstract]) OR (rehabilitation[Title/Abstract]) OR (conventional physiotherapy[Title/Abstract]) OR (conventional rehabilitation[Title/Abstract]) OR (Physical therapy[Title/Abstract]) OR (Conventional physical therapy[Title/Abstract]) OR (Inpatient therapy[Title/Abstract]) OR ("stroke rehabilitation"[MeSH Terms]) OR ("Neurological Rehabilitation"[MeSH Terms]) OR ("Exercise Therapy"[MeSH Terms]))

Appendix 2. Cochrane search strategy

MeSH descriptor: [Hand] this term only

MeSH descriptor: [Wrist] this term only

MeSH descriptor: [Hand Joints] this term only

MeSH descriptor: [Hand Strength] this term only

("Box and Block Test"):ti,ab,kw OR (BBT):ti,ab,kw OR ("Purdue Pegboard Test"):ti,ab,kw OR (PPT):ti,ab,kw OR ("Fugl-Meyer Assessment"):ti,ab,kw

(FMA):ti,ab,kw OR (Wolf motor function test):ti,ab,kw OR (WMFT):ti,ab,kw OR (grip):ti,ab,kw OR (Pinch):ti,ab,kw

(Action research arm test):ti,ab,kw OR (ARAT):ti,ab,kw OR ("Jebsen Hand Function Test"):ti,ab,kw OR (JHFT):ti,ab,kw

#1 OR 2# OR 3# OR 4# OR 5# OR 6# OR 7#

("virtual reality"):ti,ab,kw OR ("virtual reality therapy"):ti,ab,kw OR ("VR"):ti,ab,kw OR (Stimulated 3D environment):ti,ab,kw

MeSH descriptor: [Virtual Reality] this term only

MeSH descriptor: [Virtual Reality Exposure Therapy] this term only

#9 OR #10 OR #11

("chronic"):ti,ab,kw

("stroke"):ti,ab,kw OR ("post-stroke"):ti,ab,kw

MeSH descriptor: [Physical Therapy Modalities] this term only

("conventional treatment"):ti,ab,kw OR ("physiotherapy"):ti,ab,kw OR ("Physiotherapist"):ti,ab,kw OR (Inpatient therapy):ti,ab,kw OR (Exercises therapy):ti,ab,kw

#15 OR #16

#8 AND #12 AND #13 AND #14 AND #17

Appendix 3. PEDro search strategy

Abstract & Title: virtual reality, stroke, chronic, upper limb, physiotherapy*

Body part: hand or wrist

Subdiscipline: neurology

Appendix 4. ICTRP

Search: Virtual reality AND stroke AND chronic AND upper limb

Filters: With result only

Appendix 5. Ct.gov

Condition or disease: Stroke AND chronic

Other terms: Hand OR finger

Intervention: Virtual reality AND (physiotherapy OR conventional therapy OR occupational therapy)

Filters: Studies with results only

DECLARATION OF CONFLICTING INTERESTS

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