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Effect of virtual reality rehabilitation on motor function in patients with stroke: A narrative review

Miguel Barbosa Castro Ferreira

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Orientado por:

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Michele dos Santos Gomes da Rosa

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Trabalho Final do Mestrado Integrado em Medicina, apresentado para cumprimento dos requisitos necessários à obtenção do grau de Mestre em Medicina, realizado sob a orientação do Prof. Dr. Gabriel Miltenberger Miltenyi e da Dr.ª Michele dos Santos Gomes da Rosa, Investigadora na Clínica Universitária de Cardiologia, dirigida pela Prof.ª Doutor Fausto J. Pinto.

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RESUMO

Introdução: O acidente vascular cerebral é uma das principais causas de morte e incapacidade no mundo, sendo descrita como uma epidemia global. Défices motores causados por esta etiologia, afetam as tarefas diárias, bem como, a atividade profissional destas pessoas, resultando num dia-a-dia repleto de obstáculos. Desta forma, a reabilitação tem um papel fulcral, na melhoria destas queixas e consequentemente na qualidade de vida. A realidade virtual é uma ferramenta, que nos recentes anos tem vindo a ganhar um papel cada vez de maior importância para estes doentes. Nesta revisão narrativa, pretendemos comparar a reabilitação convencional com a reabilitação baseada na realidade virtual e perceber, desta forma, se existe benefício na combinação de ambas.

Métodos: A nossa estratégia de pesquisa consistiu na pesquisa de ensaios clínicos randomizados em três diferentes plataformas (PubMed, sci-Elo e medRxiv), publicados nos últimos 10 anos cujo objetivo primário se focasse na função motora dos membros superiores. Usamos as seguintes palavras-chave como ponto de partida para a pesquisa de artigos: “Virtual Reality”, “rehabilitation”, “stroke”. Após ser aplicada a estratégia de pesquisa acima mencionada, obtivemos um total de 100 artigos. Após análise destes mesmos 100 artigos, somente 26 tinham os critérios necessários para a sua utilização na revisão, com uma amostra total de 1382 pacientes envolvidos nesta revisão de narrativa.

Resultados: Como referido previamente, dos 100 artigos, somente 26 foram utilizados para a construção desta revisão narrativa. Os 74 artigos foram excluídos por não preencherem os critérios necessários para a sua inclusão. O facto do artigo não se focar na função motora do membro superior, foi a principal causa de exclusão de artigos. Outras razões como duplicados, não ter acesso livre, não focar o seu estudo na reabilitação do acidente vascular cerebral e não focar no estudo da realidade virtual também foram motivos para exclusão.

Conclusão: Devido a inúmeras variáveis entre os diferentes ensaios, é impossível a conclusão de possíveis conexões entre a intervenção e os resultados obtidos. Sugere-se

a realização de estudos em que certas variáveis como a intervenção realizada ao grupo de intervenção, o número de sessões, a duração das mesmas, sejam homogeneizados.

Palavras-chave: Virtual Reality, Rehabilitation, Stroke.

ABSTRACT

Introduction: Stroke is one of the leading causes of death and disability and has been described as a worldwide epidemic. Motor function deficits due to stroke affect the patients' performance in daily tasks as well as in their jobs, which results in an increased difficulty in their everyday life. This way, rehabilitation in these patients plays an important role trying to improve their motor function and therefore their quality of life. Virtual reality, in recent years, has been increasingly more popular in this type of patients. In this narrative review, we aim to compare conventional therapy versus virtual reality-based therapy and find out if there is any kind of benefit in combining conventional therapy with virtual reality-based therapy.

Methods: Our search strategy consisted in searching for randomized controlled trials published in the last 10 years with the primary outcome focusing on upper limb motor function, in three different platforms (PubMed, sci-Elo and medRxiv) using the following keywords: “virtual reality”, “rehabilitation”, “stroke”. After applied our search strategy we ended up with a total of 100 articles. After analyzing the 100 trials, only 26 of them met the necessary criteria to take part of this review, with a total sample of 1382 patients involved in the narrative review.

Results: As previously mentioned, of the 100 articles, only 26 were used to build this narrative review. 74 articles excluded for not meeting the necessary criteria to make part of this review. The fact that the article did not focus on the motor function of the upper limb was the main reason for the exclusion of articles. Other reasons such as duplicates, not having open access, not focusing their study on stroke rehabilitation and not focusing on the study on virtual reality were also reasons for exclusion.

Conclusion: Due to numerous variables between the different trials, it is impossible to conclude possible connections between the intervention and the results obtained. It is suggested that studies should be carried out with certain variables, such as the intervention carried out in the intervention group, the number of sessions, the duration of the sessions, homogenized.

Key words: Virtual Reality, Rehabilitation, Stroke.

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ABBREVIATIONS LIST

VR - Virtual Reality

CT – Conventional Therapy

ADL - Activities of daily living

RCT – Randomized controlled trial

DALYs - Disability-adjusted life-years

MMSE – Mini mental state examination

FMA – Fugl-Meyer Assessment

BBT – Box-blocks test

INTRODUCTION

Description of the condition

Stroke is defined by World Health Organization as rapidly developing clinical signs of focal (at times global) disturbance of cerebral function lasting more than 24 h or leading to death with no apparent cause other than that of vascular origin (1). Furthermore, stroke is the second leading cause of death globally and is also one of the main causes of disability worldwide. The effects of a stroke may include sensory, motor and cognitive impairment as well as a reduced ability to perform self-care and participate in social and community activities (2).

In 2015 in the United States of America from the 795,000 new sufferers of stroke, 26% remain disabled in basic activities of daily living and 50% have reduced mobility due to hemiparesis (3). Aphasia and depression are other frequent causes of disability (4). In Portugal, the latest numbers from 2017 showed that stroke was responsible for 10,6% (11.270) of the total deaths that year (5) and is the major cause of disability and disability-adjusted life-years (DALYs).

Description of the intervention

Nowadays, technological resources have been used in several areas, being medicine one of them, this way combining the expertise from both medicine and engineering, we are able to produce better rehabilitation conditions to patients with stroke, but also many other diseases like, Parkinson's' disease, cerebral palsy, down syndrome and multiple sclerosis. VR is defined as a set of informatics technologies that create interactive environments that involve the user while simulating the real world. These systems consist of specific software programs and input-output peripherals that reproduce complex and immersive experiences (6).

The key concepts of virtual reality are immersion and presence, immersion describes the degree of which VR systems can deliver experiences that are extensive (i.e., multimodality sensory stimuli), presence is a psychological, perceptual, and "feel of being there.", there are other concepts like surrounding (i.e., omnidirectional stimuli),

inclusive (i.e., no external stimuli from the physical environment), vivid (i.e., richness of a sensory information) and matching (i.e., user movement and system information match) (7).

The purpose of this review

Rehabilitation of a patient is a process that involves the knowledge of the medical professionals such as physicians, nurses and therapists, regarding the health condition and the repercussion it has on the life of the individual, as well as a broad scientific knowledge about the functioning of the human body, so that consistent decisions could be made (8).

The well-being of the patient is always the major concern while practicing medicine, so we should always strive to bring innovation to achieve our primary goal. Although, conventional rehabilitation, based on repetitive task training, has shown benefits, virtual reality regulates activity difficulty according to the patient's true abilities and potentialities and controls performance with visual and auditory feedback. Moreover, these systems potentiate the quality of rehabilitation sessions, as they provide the opportunity to propose playful activities, thus increasing motivation and involvement (6).

A purported benefit of virtual reality is how motivational strategies, in the form of "gamification", can be incorporated into training paradigms reinforcing adherence to repetitive high-dose functional training. These strategies are composed of feedback systems that engage the user in on-screen objectives, immersing the user in goal-driven behavior linked to rehabilitation exercises. For some, this immersion can provide patients with a welcome break from the monotony of therapy and increase exercise output (10).

Virtual tasks have been described as more interesting and enjoyable by both children and adults, thus obtaining a higher number of repetitions, with positive results on therapist compliance and patient functional outcomes (6). Although its research in rehabilitation is becoming more prevalent as technology becomes more accessible and affordable, the use of virtual reality is not yet commonplace in clinical rehabilitation

settings. However, gaming consoles are ubiquitous and so researchers and clinicians are turning to low-cost commercial gaming systems as an alternative way of delivering virtual reality (9).

OBJECTIVES:

In this review the aim is fully understand the benefits of using virtual-based rehabilitation, comparing it we the conventional rehabilitation on the motor function of the upper limb after a stroke. Finally, check if there is any benefit in combining conventional therapy with virtual reality-based therapy.

METHODS

Inclusion criteria

Type of study

We included only randomized controlled trials and looked for trials which compared virtual-based rehabilitation with the conventional one or with no intervention at all. Studies with cross-over design or that compared two different types of virtual reality were not included.

Type of participants

The participants in these studies all had a diagnosis of stroke and older than 18. Also, all patients with any kind of visual or auditive problems were excluded.

Type of intervention

As a criterion all the studies selected should have used virtual reality with different grades of immersion, from non-immersive to immersive.

Comparison:

In the control group we analyzed trials in which patients had conventional rehabilitation or no rehabilitation at all.

Outcomes

We aimed to evaluate the rehabilitation of the upper limb after a stroke, in this way, was selected a few scales to measure that such as Fugl-Meyer Assessment, Wolf motor function test, box and block test, among others.

Search strategy

For the search of all the articles I investigated some of the most used online platforms: PubMed, SciElo and MEdrxiv. I used a few keywords “Virtual reality, Rehabilitation, Stroke” in order to search for the included articles. I included only Randomized Controlled Trials from the year 2010 on.

Table 1 - Search strategy.

PubMed	(("virtual reality"[MeSH Terms] OR ("virtual"[All Fields] AND "reality"[All Fields]) OR "virtual reality"[All Fields]) AND ("stroke rehabilitation"[MeSH Terms] OR ("stroke"[All Fields] AND "rehabilitation"[All Fields]) OR "stroke rehabilitation"[All Fields] OR ("rehabilitation"[All Fields] AND "stroke"[All Fields]) OR "rehabilitation stroke"[All Fields])) AND ((randomizedcontrolledtrial[Filter]) AND (english[Filter] OR portuguese[Filter]) AND (2010:2020[pdat]))

Study eligibility

The exclusion criteria were:

1) Trials that did not use VR in rehabilitation.
2) Trials that had only comparison between groups of different types of virtual reality-based rehabilitation and not present a group without virtual reality-based rehabilitation.
3) Trials that present VR in rehabilitation but not aimed in stroke rehabilitation.
4) Study protocols
5) Study not aimed at the upper limb motor function.
6) No open access

RESULTS

After the search strategy methods were used, we found 100 scientific articles, and after careful evaluation only 26 articles met all the necessary criteria for their inclusion in this narrative review. Out of the 74 excluded articles, 1 was duplicated, 7 did not have an open access, 7 were study protocols, 7 were not aimed at the VR study, 8 of them did not study the stroke rehabilitation, 3 were comparing two different types of VR, 1 study did not have a control group, and finally most of the excluded trials, were not aimed at the upper limb motor function. Finally, I justify in detail the reason why the article was excluded (Attachment 1).

Studies were also teste for their quality using the Delphi List for Quality Assessment of Randomized Clinical Trials, and they also had moderate-high quality with the scores ranging from 5 to 7 (Table 3).

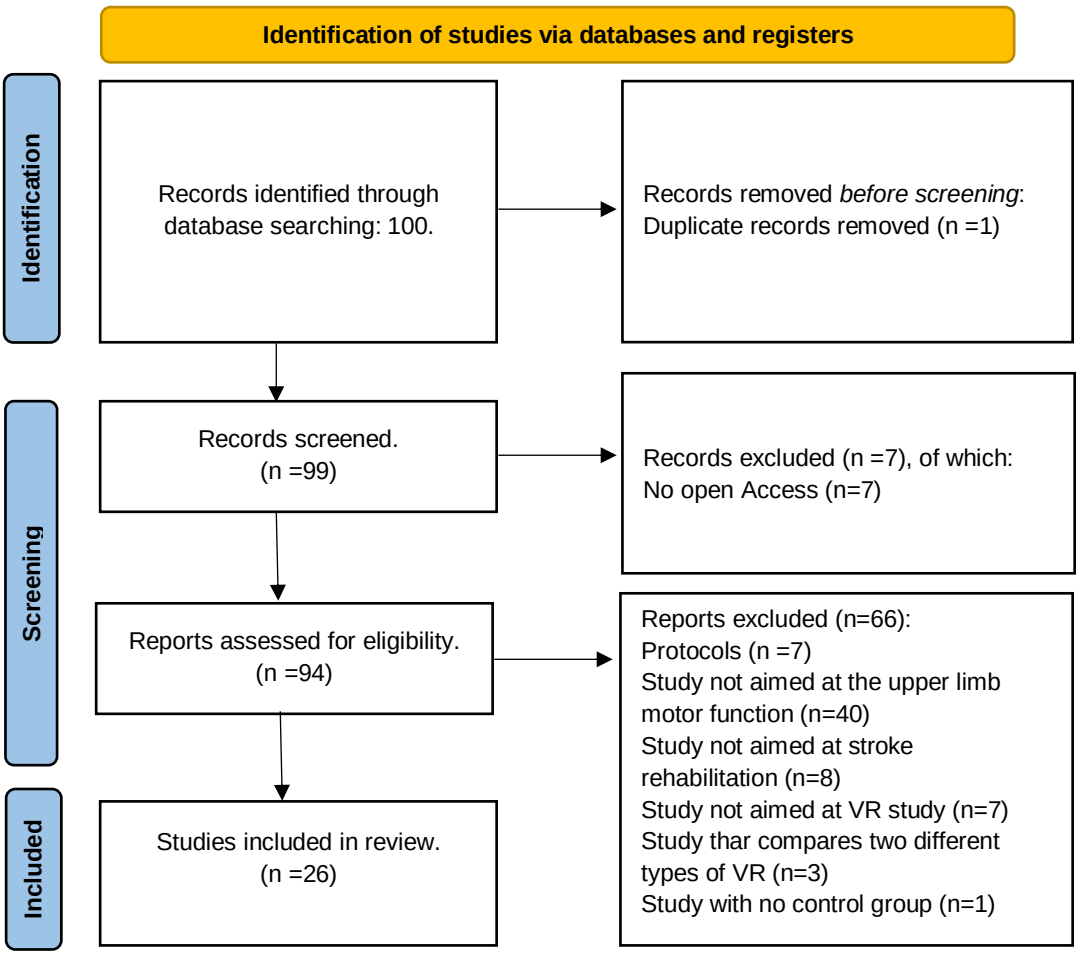

Figure 1 - Study flow diagram of systematic review.

The 26 articles were evaluated for type of study, number of the sample, objective of the study, inclusion and exclusion criteria of the participants (Table 2). The outcomes and the results were also evaluated (Table 5).

Table 2 - Characteristics of the studies include in the review.

Title	Year	Study	DOI	Language	Study Type	Number of Subjects	Objective	Inclusion criteria	Exclusion criteria
Additional virtual reality training using Xbox Kinect in Stroke survivors with hemiplegia	2013	Sin	10.1097/PHM.0b013e3182a38e40	English	RCT	40	the aim of this study was to evaluate the effect of additional training with virtual reality on the upper limb function	More than 6 months after stroke; no visual or auditory problems; active range of motion (ROM) of the shoulder, the elbow, the wrist, and the fingers is more than 10 degrees; ability to walk more than 10 m independently; not taking any medication that could influence balance or gait; and no severe cognitive disorders.	Uncontrolled blood pressure or angina, history of seizure, any intervention other than conventional therapy, or refusal to use a video game.
Arm Motor Recovery Using a Virtual Reality Intervention in Chronic Stroke: Randomized Control Trial	2012	Sandeep	10.1177/1545968312449695	English	RCT	32	The authors compared kinematic and clinical outcomes of dose-matched upper-limb training between a 3D Virtual environment and a Physical environment in chronic stroke	Age between 40 and 80 years; sustained a single ischemic or hemorrhagic stroke 6 to 60 months previously; scored 3 to 6/7 on the Chedoke-McMaster Stroke Assessment19 arm subscale; had no other neurologic or neuromuscular/orthopedic problems affecting the upper limb and trunk.	Brainstem/cerebellar lesions; comprehension difficulties, and marked apraxia, attention, or visual field deficits.
Comparison of Kinect2Scratch game-based training and therapist-based training for the improvement of upper extremity functions of patients with chronic stroke a randomized controlled single-blinded trial	2019	HUNG	10.23736/S1973-9087.19.05598-9	English	RCT	33	Create kinect2Scratch games and compare the effects of training with therapist-based training on upper extremity function of patients with chronic stroke	Clinical and imaging-based diagnosis of a unilateral stroke more than 6 months before the trial; Having active movement of the affected upper extremity; Mini mental state exam score greater than 20; Age more than 18 years	Bilateral hemispheric or cerebellar lesions, severe aphasia, significant visual field deficits or hemineglect and any conditions that would prevent adherence to the rehabilitation protocol.
Elements virtual rehabilitation improves motor, cognitive, and functional outcomes in adult stroke: evidence from a randomized controlled pilot study	2019	Jeffrey M. Rogers	10.1186/s12984-019-0531-y	English	RCT	21	The present study aims to evaluate the efficacy of Elements as a virtual rehabilitation approach for stroke survivors	Ability to communicate in English and understand and follow oral instructions; ability to maintain sitting balance unassisted.	Previous history of neurological (other than stroke), psychiatric, or developmental disorder; loss of visual acuity preventing perception of visual material; under 18 years of age. Rehabilitation staff assisted in

									the identification of eligible candidates.
Training finger individuation with a mechatronic-virtual reality system leads to improved fine motor control post-stroke	2014	Kelly O Thielbar	10.1186/1743-0003-11-171	English	RCT	14	The purpose of this study was to investigate the impact of such finger individuation training, by means of a novel mechatronic-virtual reality system, on fine motor control after stroke.	Abduction of the digits to full range of motion; touching of the tip of the thumb to the tip of the little finger; smooth reversal between full flexion and full extension of the digits.	Receiving outpatient physical or occupational therapy; had biomechanical limitations (e.g., contracture) which limited passive digit extension to 20° of finger flexion; had received a botulinum toxin (e.g., Botox®) injection less than 6 months prior to enrolment, had cognitive deficits limiting simple one-step commands, had significant upper extremity pain (rated as greater than 6/10)
Does the use of Nintendo Wii Sports TM improve arm function? Trial of Wii TM in Stroke: A randomized controlled trial and economics analysis	2016	Adie	10.1177/0269215516637893	English	RCT	209	The Trial of Wii™ in Stroke investigated the efficacy of using the Nintendo Wii Sports™ (Wii TM) to improve affected arm function after stroke.	Participants with ischaemic or haemorrhagic stroke within the last six months; arm weakness owing to stroke, defined as Medical Research Council Scale power less than 5 in any joint plane; able to manipulate the Wii TM remote control.	Severe co-morbidity that could impair participation; symptomatic shoulder subluxation; pacemaker device (possible interference from the Wii TM)
Effect of a four-week virtual reality-based training versus conventional therapy on upper limb motor function after stroke: A multicenter parallel group randomized trial	2018	Schuster-Amft C	10.1371/journal.pone.0204455	English	RCT	54	The aim of this study was to directly compare virtual reality-based training with conventional therapy.	Six months after his or her first-ever stroke (ischemic or hemorrhagic) with a persistent motor deficit of the arm and hand, indicated by a Chedoke-McMaster Stroke Assessment (CMSA) score of three or greater on the arm subscale and two or greater on the hand subscale. If one of the CMSA subscales scored seven, the difference to the other subscale had to be at least two. Patients had to be able to sit in a normal chair without armrests or backrest support and to score at least one on the Box and Block Test, which was the primary outcome measure.	Previous or current functional deficits of the arm and hand motor function not due to stroke; severe cognitive deficits indicated by a Mini-Mental State Examination score of 20 or lower; severe visual disorders; history of epileptic seizures triggered by visual stimuli within the past six months.

Effect of Leap Motion-based 3D Immersive Virtual Reality Usage on Upper Extremity Function in Ischemic Stroke Patients	2019	ÖGÜN	10.1590/0004-282X20190129	English	RCT	75	The aim of this study was to investigate the effectiveness of immersive VR on upper extremity function in patients with ischemic stroke.	Mini-Mental State Examination score ≥ 25; stroke onset between six and 24 months; a Modified Ashworth Scale score < 3; an upper extremity and hand Brunnstrom score ≥ 4.	Secondary neurological diseases; recurrent stroke; reduced or lost visual field in one or both eye(s); hemorrhagic stroke.
Effect of Virtual Reality-based Bilateral Upper Extremity Training on Upper Extremity Function after Stroke: A Randomized Controlled Clinical Trial	2016	Suhyun	10.1002/oti.1437	English	RCT	18	The aim of this study is to investigate the effect of virtual reality-based bilateral upper extremity training on paretic upper limb function and muscle strength in patients with stroke.	Diagnosis of stroke at least 6months prior; Mini-Mental State Examination (MMSE) score of 24–30; Brunnstrom recovery stages 1–4; Modified Ashworth Scale (MAS) score of an upper extremity of less than 2.	Presence of diplegia or a visual field defect; acute musculoskeletal deconditioning with pain or disability.
Effects of Kinect-based virtual reality game training on upper extremity motor recovery in chronic stroke	2018	Ayhan Aşkın	10.1080/08990220.2018.1444599	English	RCT	40	Assess the effects of Kinect-based VR training on motor recovery of the upper extremity and functional outcomes in patients with chronic stroke.	Ischemic or hemorrhagic stroke; adults (>18 years old); stroke onset>6 months; absence of cognitive, visual impairment or neglect that made it impossible to follow the instructions during treatment sessions; voluntary shoulder, elbow, and wrist movement that can perform game commands.	Clinically unstable or had concomitant neurodegenerative disorders, other intracranial diseases, history of seizure, significant medical or psychiatric illness, fixed contractures or bony deformities of the affected extremity, taking any drug that could affect balance, and severe cognitive problems (Mini-mental test score of<20/30).
Effects of virtual reality on upper extremity function and activities of daily living performance in acute stroke: A double-blind randomized clinical trial	2012	Kwon	10.3233/NRE-2012-00807	English	RCT	26	Examine the effects of conventional therapy (CT) combined with intensive virtual reality (VR) program on upper extremity function and activities of daily living (ADL) in individuals in the acute stage of stroke.	Adults who are within a three-month post-stroke period; individuals with capacity to understand and follow simple instructions; adults demonstrating 3 grades on the Manual Muscle Test (MMT) of elbow joint movement; ability to grasp and release affected hand; ability to maintain standing or sitting position independently; no visual deficit.	No reference

Effects of Virtual Reality Training using Xbox Kinect on Motor Function in Stroke Survivors: A Preliminary Study	2017	Park	10.1016/j.jstrokecerebrovasdis.2017.05.019	English	RCT	20	This study aimed to investigate the effects of VR training, using the Xbox Kinect-based game system, on the motor recovery of patients with chronic hemiplegic stroke.	Period of more than 6 months between stroke and randomization; hemiplegic stroke as diagnosed by a neurologist; a total score of 21 or greater on the Mini–Mental State Examination (MMSE); no problems with auditory or visual functioning; an ability to walk more than 10 m with or without assistive devices; not taking any medication that could influence balance; stable vital signs; and a capacity to provide informed consent.	Uncontrolled blood pressure or angina; musculoskeletal impairments of the lower extremity; psychological conditions; or the refusal to use a video game.
Effects of virtual reality-based rehabilitation on distal upper extremity function and health-related quality of life: a single blinded, randomized controlled trial	2016	Shin	10.1186/s12984-016-0125-x	English	RCT	46	The purpose of the present study was to examine the effects of VR-based rehabilitation combined with standard occupational therapy on distal upper extremity function and health-related quality of life and compare the findings to those of amount-matched conventional rehabilitation in stroke survivors.	First-ever ischemic or hemorrhagic stroke; complaints of unilateral upper extremity functional deficits after stroke; presence of a score of at least 2 points on the medical research council scale [14] for wrist flexion/extension or forearm pronation/ supination, as the SG system can be operated only with volitional movements and does not involve external assistance.	Age <18 years; uncontrolled hypertension, unstable angina, recent myocardial infarction, or any history of seizure; predisposing psychological disorders that could impede participation; neurological disorders that cause motor deficits, such as Parkinson's disease and peripheral neuropathy; severe aphasia resulting in communication difficulties that could influence the intervention and outcome measures; cognitive impairment resulting in cooperation difficulties (a score of ≤24 in the Mini-Mental State Examination) [15]; severe pain impeding upper extremity rehabilitation (numeric pain rating scale score ≥ 7).
Efficacy and safety of non-immersive virtual reality exercising in stroke rehabilitation (EVREST): a randomised, multicentre, single-blind, controlled trial	2016	Saposnik	10.1016/S1474-4422(16)30121-1.	English	RCT	141	The aim was to compare the safety and efficacy of virtual reality with recreational therapy on motor recovery in patients after an acute ischaemic stroke.	Patients aged 18–85 years who had a first-time ischaemic stroke within 3 months of enrolment; mild-to-moderate motor disability (defined as Chedoke-McMaster Stroke Assessment stage >3); Diagnosis of acute stroke was confirmed by neuroimaging (CT or MRI)	No Reference

Efficacy of a Virtual Reality Commercial Gaming Device in Upper Limb Recovery after Stroke: A Randomized, Controlled Study	2016	Kong	10.1080/10749357.2016.1139796	English	RCT	105	Compare the efficacy of a virtual reality commercial gaming device, Nintendo Wii (NW) with conventional therapy and customary care in facilitating upper limb recovery after stroke.	Age 21–80 years; First clinical stroke, ischemic or hemorrhagic, with diagnosis of stroke confirmed on CT/MRI brain scan; Less than 6 weeks after stroke onset; Upper limb weakness of Medical Research Council (MRC) motor power of grade 2–4 motor power in either the shoulder, elbow, or the fingers of the hemiplegic upper extremity; Subject can understand simple instructions and learn	Recurrent stroke; History of epilepsy; Presence of arthritis or pain in the affected upper limb restricting repetitive exercises; Severe aphasia or cognitive impairment, or other psychiatric illnesses that limits ability to participate or give consent.
Efficacy of Virtual Reality Combined with Real Instrument Training for Patients with Stroke: A Randomized Controlled Trial	2019	Oh	10.1016/j.apmr.2019.03.013	English	RCT	31	Investigate the efficacy of real instrument training in virtual reality (VR) environment for improving upper-extremity and cognitive function after stroke.	First-episode stroke, as demonstrated by brain computed tomography or magnetic resonance imaging; evaluated for a period of 6months after stroke onset; age between 20 and 85 years; patients with unilateral paralysis or paresis, with a Fugl- Meyer assessment upper-extremity scale (FMA-UE) score >18, indicating mild-to-moderate dysfunction; substantial cooperation to complete the assessment.	Serious or unstable medical problems; history of other neurologic diseases and/or psychiatric disorders; insufficient cognitive and language functions, with a Korean Mini-Mental State Examination (K-MMSE) score <19.
Feasibility, Safety and Efficacy of a Virtual Reality Exergame System to Supplement Upper Extremity Rehabilitation Post-Stroke: A Pilot Randomized Clinical Trial and Proof of Principle	2019	Nahid	10.3390/ijerph17010113	English	RCT	18	The goal of this study was to examine the safety and feasibility of providing additional therapy using an exergame system and assess its preliminary clinical e efficacy.	Had an ischemic or hemorrhagic stroke for the first time; having residual mild to moderate UE impairment (score 3–6 on the Chedoke–McMaster arm component [17]); being in subacute or chronic stage; receiving usual out-patient rehabilitation services at one of the two selected rehabilitation sites, i.e., Institut de réadaptation Gingras-Lindsay-de-Montréal and Jewish Rehabilitation Hospital, all located in the greater Montreal area in Canada.	Having severe cognitive or communication deficits; having visual impairments; having any medical contraindication for shoulder movements; having severe balance deficits limiting sitting safely independently; having previous UE impairment limiting potential recovery; having any other impairment that limited use of the VR system.

Mobile Game-based Virtual Reality Program for Upper Extremity Stroke Rehabilitation	2018	Yoon-Hee	10.3791/56241	English	RCT	24	In this study, a mobile VR upper extremity rehabilitation program using game applications was developed.	Diagnosed with ischemic stroke; had the ability to follow a one-step command; had the medical stability to participate in active rehabilitation; had upper extremity impairment	Delirium, confusion, or other severe consciousness problems; suffered from uncontrolled medical conditions; were unable to follow commands because of severe cognitive impairment; had a visual disturbance; had poor sitting balance.
Mobile game-based virtual reality rehabilitation program for upper limb dysfunction after ischemic stroke	2016	Yoon-Hee	10.3233/RNN-150626	English	RCT	24	The objective of the present study was to develop a mobile game-based upper extremity VR program for patients who have experienced stroke, and to evaluate the feasibility and effectiveness of the program.	Diagnosis of ischemic stroke; the ability to follow a one-step command; clinical stability allowing participation in active rehabilitation; upper extremity impairment with a Brunnstromstage between 1 (flaccidity present and no movements of the limbs can be initiated) and 5 (more difficult movement combinations are possible as the basic limb synergies lose their dominance over motor actions)	Had delirium, confusion, or other severe consciousness problems; suffered from uncontrolled medical conditions; were unable to follow commands because of severe cognitive impairment; had visual disturbance, such as visual field defects and visuospatial neglect; had poor sitting balance.
Reinforced Feedback in Virtual Environment for Rehabilitation of Upper Extremity Dysfunction after Stroke: Preliminary Data from a Randomized Controlled Trial	2014	Kiper	10.1155/2014/752128	English	RCT	44	To study whether the reinforced feedback in virtual environment (RFVE) is more effective than traditional rehabilitation (TR) for the treatment of upper limb motor function after stroke, regardless of stroke etiology (i.e., ischemic, hemorrhagic).	Diagnosis of a first stroke (ischemic or hemorrhagic) occurring at last 1 year before the enrolment and never treated before with reinforced feedback in virtual environment	clinical evidence of severe cognitive impairment (i.e., a score lower than 24 points at the Mini-Mental State Examination), clinical history of neglect, the presence of complete hemiplegia (i.e., Fugl-Meyer upper extremity scale = 0 pts.), sensory disorders (i.e., a score lower than 16 points at sensibility subitem of the Fugl-Meyer scale), and history of traumatic injuries (e.g., fracture, joint dislocation with

									permanent dysmorphism after trauma) impairing the upper limb motor function.
Virtual reality-based rehabilitation speeds up functional recovery of the upper extremities after stroke: A randomized controlled pilot study in the acute phase of stroke using the Rehabilitation Gaming System	2011	Cameirão	10.3233/RNN-2011-0599	English	RCT	19	Given the incidence of stroke, the need has arisen to consider more self-managed rehabilitation approaches. A promising technology is Virtual Reality (VR). Thus far, however, it is not clear what the benefits of VR systems are when compared to conventional methods. Here we investigated the clinical impact of one such system, the Rehabilitation Gaming System (RGS), on the recovery time course of acute stroke. RGS combines concepts of action execution and observation with an automatic individualization of training.	First episode stroke, acute stroke within three weeks post-stroke at baseline; severe to moderate deficit of the paretic upper extremity (2≤MRC≤3) (MRC, 1976); no severe to moderate aphasia (Rosselli et al., 1990); no other cognitive deficits as assessed by the Mini-Mental State Examination (Folstein et al., 1975), cooperation, and age≤80 years.	No reference
Virtual reality for upper extremity rehabilitation in early stroke: a pilot randomized controlled trial	2014	Yin	10.1177/0269215514532851	English	RCT	23	To investigate the effect of virtual reality (VR) rehabilitation on upper extremity motor performance of patients with early stroke.	Medical stability to participate in active rehabilitation; above 21 years old; able to stand unsupported for 30 seconds; Fugl-Meyer Assessment for the upper extremity (FMA)10 score of below 62; a Mini Mental State Examination (MMSE)11 score of above 20.	Had epilepsy, photophobia or known side effects from watching digital media; were pregnant; had implanted electronic devices including pacemakers or defibrillators; had joint pain that could limit participation; had severe visual deficits; presented with

									spasticity score of more than 2 in the affected limb quantified by the Modified Ashworth scale.
Virtual reality for upper limb rehabilitation in sub-acute and chronic stroke: a randomized controlled trial	2018	Kiper P	10.1016/j.apmr.2018.01.023	English	RCT	136	To evaluate the effectiveness of reinforced feedback in virtual environment (RFVE) treatment combined with conventional rehabilitation (CR) in comparison with CR alone, and to study whether changes are related to stroke aetiology (i.e. ischemic or hemorrhagic).	First episode of stroke due to both ischemic and hemorrhagic aetiologies (figure 1). Subjects who had a stroke onset up to twelve months before enrolment were included in the study	Cognitive impairment (defined as score lower than 24 at the Mini-Mental State Examination – MMSE) [20], having previously received RFVE treatment, presence of apraxia (defined as a score lower than 62 points at the De Renzi test) [21], impairment of verbal comprehension (defined as a score higher than 40 errors at the Token test) [22], evidence in the clinical history of neglect, upper extremity complete hemiplegia (score = 4 points in the upper-limb sub-item of the National Institute of Health Stroke Scale) [23], presence of upper limb sensory disorders (defined as < 1 points in items shoulder, elbow, wrist and thumb at the sensitivity section of the Fugl-Meyer scale), fracture, joint dislocation
Virtual reality in the rehabilitation of the arm after hemiplegic stroke: a randomized controlled pilot study	2012	Crosbie	10.1177/0269215511434575	English	RCT	18	To assess the feasibility of a trial to investigate the effectiveness of virtual reality-mediated therapy compared to conventional physiotherapy in the motor rehabilitation of the arm following stroke, and to provide data for a power analysis to determine numbers for a future main trial.	Adult aged 18–85 years; 6–24 months following a first stroke and able to follow a two-step command	mental score test of less than 7/10; a star cancellation score of less than 48/52; scored less than 25 out of 100 on the upper limb Motricity Index; had comorbid conditions affecting their rehabilitation potential (e.g. cardiac, respiratory or arthritic problems) and reported arm pain on a visual analogue scale of >6/10. A score of 0–25 on the Motricity Index is deemed to indicate

									very severe motor loss. anyone with a cardiac pacemaker as the electromagnetic motion tracker used within the virtual reality system might interfere with such devices.
Virtual Reality in Upper Extremity Rehabilitation of Stroke Patients: A Randomized Controlled Trial	2018	Afsar	10.1016/j.jstrokecerebrovasdis.2018.08.007	English	RCT	42	We aimed to evaluate the effect of the Microsoft Xbox 360 Kinect video game system on upper limb motor functions for subacute stroke patients.	a first episode of unilateral stroke with hemiparesis; stroke duration less than 6 months and more than 1 month; medically stable enough to participate in active rehabilitation; mild-to-moderate motor upper extremity deficits (Brunnstrom stage for the upper extremity >= 3); ability to execute at least 20 degrees of active shoulder flexion and abduction against gravity; no problems with auditory or visual functioning; a total score of 23 or greater on the Mini Mental State Examination.	Severe conditions such as uncontrolled blood pressure or angina, history of epilepsy, any intervention other than conventiona ltherapy, or the refusal to play a video game.
Virtual Reality Training for Upper Extremity in Subacute Stroke (VIRTUES)	2017	Brunner	10.1212/WNL.0000000000004744	English	RCT	120	To compare the effectiveness of upper extremity virtual reality rehabilitation training (VR) to time-matched conventional training (CT) in the subacute phase after stroke.	All patients with a diagnosis of stroke (cerebral infarction or hemorrhage) admitted to the participating rehabilitation centers	Severe cognitive deficits defined as ,20 on the Mini-Mental State Examination; conditions limiting the ability to comply with the treatment regimen such as orthopedic impairment limiting mobility substantially or causing pain in the affected arm or visual disorders.
Virtual rehabilitation via Nintendo Wiit and conventional physical therapy effectively treat post-stroke hemiparetic patients	2015	da Silva Ribeiro	10.1179/1074935714Z.0000000017	English	RCT	30	Compare the effect of a rehabilitation treatment using the Nintendo Wii (NW) with conventional physical therapy (CPT) to improve the sensorimotor function and quality of life for	Male or female, aged between 18 and 60 years of age to avoid the effect of advanced age on the results, with an exclusive diagnosis of stroke (performed by a neurologist based on computerized tomography or magnetic resonance imaging) presenting with hemiparesis; able to ambulate and hold the game controller without assistive devices. The last	Associated disorders such as hemineglect or pusher syndrome; an intellectual disability that made it difficult to understand the games, or a history of orthopedic diseases that promoted dysfunction in the upper limbs (ULs); lower limbs (LLs), or both that prevented the performance of the proposed activity.

							post-stroke hemiparetic patients.	stroke episode occurred at least 6 months prior to the study.	

Table 3 - Delphi List for Quality Assessment of Randomized Clinical Trials.

Criteria	Evaluation
1. Treatment allocation: Was a method of randomization?	Yes (1)/ No (0)
2. Treatment allocation: Was the treatment allocation concealed?	Yes (1)/ No (0)
3. Were the groups similar at baseline regarding the most important prognostic indicators?	Yes (1)/ No (0)
4. Were the eligibility criteria specified?	Yes (1)/ No (0)
5. Was the outcome assessor blinded?	Yes (1)/ No (0)
6. Was the care provider blinded?	Yes (1)/ No (0)
7. Was the patient blinded? [omitted]	Yes (1)/ No (0)
8. Were point estimates and measures of variability presented for the primary outcome measures?	Yes (1)/ No (0)
9. Did the analyses include an intention-to-treat analysis?	Yes (1)/ No (0)

Table 4 – Delphi List Result for each Study

Title	Year	Study	Delphi List
Additional virtual reality training using Xbox Kinect in stroke survivors with hemiplegia	2013	RCT	7
Arm Motor Recovery Using a Virtual Reality Intervention in Chronic Stroke. Randomized Control Trial	2014	RCT	7
Comparison of Kinect2Scratch game-based training and therapist-based training for the improvement of upper extremity functions of patients with chronic stroke a randomized controlled single-blinded trial	2015	RCT	6
Does the use of Nintendo Wii improve arm function Trial of Wii TM in Stroke a randomized controlled trial and economics analysis	2016	RCT	6
Effect of a four-week virtual reality-based training versus conventional therapy on upper limb motor function after stroke: A multicenter parallel group randomized trial	2018	RCT	5
Effect of Leap Motion-based 3D Immersive Virtual Reality Usage on Upper Extremity Function in Ischemic Stroke Patients	2019	RCT	7
Effect of Virtual Reality-based Bilateral Upper Extremity Training on Upper Extremity Function after Stroke: A Randomized Controlled Clinical Trial	2016	RCT	7
Effects of Kinect-based virtual reality game training on upper extremity motor recovery in chronic stroke	2018	RCT	7
Effects of virtual reality on upper extremity function and activities of daily living performance in acute stroke: A double-blind randomized clinical trial	2012	RCT	6
Effects of Virtual Reality Training using Xbox Kinect on Motor Function in Stroke Survivors: A Preliminary Study	2017	RCT	5
Effects of virtual reality-based rehabilitation on distal upper extremity function and health-related quality of life: a singleblinded, randomized controlled trial	2016	RCT	7
Efficacy and safety of non-immersive virtual reality exercising in stroke rehabilitation (EVREST): a randomised, multicentre, single-blind, controlled trial	2016	RCT	5
Efficacy of a Virtual Reality Commercial Gaming Device in Upper Limb Recovery after Stroke: A Randomized, Controlled Study	2016	RCT	5
Efficacy of Virtual Reality Combined with Real Instrument Training for Patients with Stroke: A Randomized Controlled Trial	2019	RCT	6
Feasibility, Safety and efficacy of a Virtual Reality Exergame System to Supplement Upper Extremity Rehabilitation Post-Stroke: A Pilot Randomized Clinical Trial and Proof of Principle	2020	RCT	5
Mobile Game-based Virtual Reality Program for Upper Extremity Stroke Rehabilitation	2018	RCT	6
Mobile game-based virtual reality rehabilitation program for upper limb dysfunction after ischemic stroke	2016	RCT	6
Reinforced Feedback in Virtual Environment for Rehabilitation of Upper Extremity Dysfunction after Stroke: Preliminary Data from a Randomized Controlled Trial	2014	RCT	6

Training finger individuation with a mechatronic-virtual reality system leads to improved fine motor control post-stroke	2014	RCT	6
Virtual reality-based rehabilitation speeds up functional recovery of the upper extremities after stroke: A randomized controlled pilot study in the acute phase of stroke using the Rehabilitation Gaming System	2011	RCT	5
Virtual reality for upper extremity rehabilitation in early stroke: a pilot randomized controlled trial	2014	RCT	6
Virtual reality for upper limb rehabilitation in sub-acute and chronic stroke: a randomized controlled trial	2018	RCT	5
Virtual reality in the rehabilitation of the arm after hemiplegic stroke: a randomized controlled pilot study	2012	RCT	7
Virtual Reality in Upper Extremity Rehabilitation of Stroke Patients: A Randomized Controlled Trial.	2018	RCT	5
Virtual Reality Training for Upper Extremity in Subacute Stroke (VIRTUES)	2017	RCT	6
Virtual rehabilitation via Nintendo Wii and conventional physical therapy effectively treat post-stroke hemiparetic patients	2015	RCT	7

Table 5 – Variables and results of the included studies.

Year/author	Tittle	DOI	N	Outcomes	Results
2013/HyeonHui Sin	Additional Virtual Reality Training Using Xbox Kinect in Stroke Survivors with Hemiplegia	10.1097/PHM.0b013e3182a38e40	40	Intervention group: VR+CT Virtual reality device: Xbox Number of sessions: 18 Duration of sessions: 30 mins of VR + 30 mins of CT Outcome measure: FMA and BBT Time since the onset of stroke: 7.22 months	Additional VR training using Xbox Kinect, a home video game device not intended as a tool for rehabilitation, can improve the functioning of the upper extremity in post-stroke survivors.
2012/ Sandeep K	Arm Motor Recovery Using a Virtual Reality Intervention in Chronic Stroke: Randomized Control Trial	10.1177/1545968312449695	32	Intervention group: VR Virtual reality device: 3D VE (CAREN) simulated a supermarket scene. Number of sessions: 12 Duration of sessions: 45 min Outcome measure: FMA and RPSS Time since the onset of stroke: no reference	VE training led to more changes in the mild group and a motor recovery pattern.
2019/Jen-Wen HUNG	Comparison of Kinect2Scratch game-based training and therapist-based training for the improvement of upper extremity functions of patients with chronic stroke a randomized controlled single-blinded trial	10.23736/S1973-9087.19.05598-9	33	Intervention group: VR Virtual reality device: kinect2Scratch (Microsoft Kinect controller) (several types of game) Number of sessions: 24 Duration of sessions: 30 minutes Outcome measure: PPS Time since the onset of stroke: no reference	Similar results between the intervention and the control group

2016/Katja Adie	Does the use of Nintendo Wii Sports TM improve arm function? Trial of Wii TM in Stroke: A randomized controlled trial and economics analysis	10.1177/0269215516637893	209	Intervention group: VR Virtual reality device: Nintendo Wii Number of sessions: 42 Duration of sessions: 45 minutes Outcome measure: Action Research Arm Test Time since the onset of stroke: At least 6 months	There was no significant difference in the primary outcome of affected arm function
2018/Corina Schuster-Amft	Effect of a four-week virtual reality-based training versus conventional therapy on upper limb motor function after stroke: A multicenter parallel group randomized trial	10.1371/journal.pone.0204455.t001	54	Intervention group: VR Virtual reality device: Simulation platform: Template for Intervention Description and Replication (TIDieR) Number of sessions: 16 Duration of sessions: 45 minutes Outcome measure: Box and Block Test Time since the onset of stroke: no reference	Patients in the experimental and control group showed similar effects
2019/Muhammed Nur ÖGÜN	Effect of Leap Motion-based 3D Immersive Virtual Reality Usage on Upper Extremity Function in Ischemic Stroke Patients	10.1590/0004-282X20190129	75	Intervention group: VR Virtual reality device: device to play task-oriented games that focused on gripping and handling of objects with arm and forearm motion and stability. Number of sessions: 18 Duration of sessions: 60 minutes Outcome measure: FMA+ARAT. Time since the onset of stroke: no reference	In both groups (intervention and control) both outcome measures showed an improvement with the time.

2016/ Suhyun Lee	Effect of Virtual Reality-based Bilateral Upper Extremity Training on Upper Extremity Function after Stroke: A Randomized Controlled Clinical Trial	10.1002/oti.1437	18	Intervention group: VR Virtual reality device: an upper extremity training program. was established using animation designed to provide visual feedback in a VR environment. Number of sessions: 18 Duration of sessions: 30 minutes Outcome measure: Box and Block test Time since the onset of stroke: no reference	VRBT group demonstrated significant. improvements in upper extremity function
2018/Ayhan Aşkın	Effects of Kinect-based virtual reality game training on upper extremity motor recovery in chronic stroke	10.1080/08990220.2018.1444599	40	Intervention group: VR + CT Virtual reality device: Xbox Kinect (Xbox 360, Microsoft, Redwood, WA, USA) was used for training. Number of sessions: 40 sessions intervention group, 20 control group Duration of sessions: 60 minutes Outcome measure: FMA Time since the onset of stroke: 6 or plus months	results suggest that the adjunct use of Kinect-based VR training may contribute to the improvement of UE motor function and AROM in chronic stroke patients.
2012/Jae-Sung Kwon	Effects of virtual reality on upper extremity function and activities of daily living performance in acute stroke: A double-blind randomized clinical trial	10.3233/NRE-2012-00807	26	Intervention group: VR + CT Virtual reality device: IREX VR system. This VR system consists of a television monitor, a video camera, cyber gloves and virtual objects, and scenes displayed on a back screen. Number of sessions: 20	This study observed that VR training has the advantage of improving intended arm function during intensive training for individuals in the acute stage of stroke.

				Duration of sessions: 100 minutes Outcome measure: FMA+FMT Time since the onset of stroke: 3 or plus months	
2017/Dae-Sung Park	Effects of Virtual Reality Training using Xbox Kinect on Motor Function in Stroke Survivors: A Preliminary Study	10.1016/j.jstrokecerebrovasdis.2017.05.019	20	Intervention group: VR + CT Virtual reality device: Xbox Kinect-based games Number of sessions: 20 Duration of sessions: 60 minutes Outcome measure: FMA+BBS Time since the onset of stroke: 6 or plus months	the use of additional VR training with the Xbox Kinect gaming system as an effective therapeutic approach for improving motor function during stroke rehabilitation.
2016/Joon-Ho Shin	Effects of virtual reality-based rehabilitation on distal upper extremity function and health-related quality of life: a single blinded, randomized controlled trial	10.1186/s12984-016-0125-x	46	Intervention group: VR + CT Virtual reality device: The RAPAEL Smart Glove™ Number of sessions: 20 Duration of sessions: 30 minutes Outcome measure: FMA Time since the onset of stroke: 6 or plus months	VR-based rehabilitation combined with standard occupational therapy might be more effective than amount-matched conventional rehabilitation for improving distal upper extremity function

2016/Gustavo Saposnik	Efficacy and safety of non-immersive virtual reality exercising in stroke rehabilitation (EVREST): a randomized, multicenter, single-blind, controlled trial	10.1016/S1474-4422(16)30121-1.	141	Intervention group: VR + CT Virtual reality device: Nintendo Wii gaming system Number of sessions: 10 Duration of sessions: 60 minutes Outcome measure: WMFT Time since the onset of stroke: 3 or plus months	non-immersive virtual reality as an add-on therapy to conventional rehabilitation was not superior to a recreational activity intervention in improving motor function
2016/Keng-He Kong	Efficacy of a Virtual Reality Commercial Gaming Device in Upper Limb Recovery after Stroke: A Randomized, Controlled Study	10.1080/10749357.2016.1139796	105	Intervention group: VR + CT Virtual reality device: Nintendo Wii gaming system Number of sessions: 12 sessions of VR + 15 of CT. Duration of sessions: 60 minutes Outcome measure: FMA Time since the onset of stroke: 6 or plus weeks	Twelve sessions of augmented upper limb exercises via NW gaming or conventional therapy over a 3-week period was not effective in enhancing upper limb motor recovery compared to control.
2019/Young-Bin Oh	Efficacy of Virtual Reality Combined with Real Instrument Training for Patients with Stroke: A Randomized Controlled Trial	10.1016/j.apmr.2019.03.013	31	Intervention group: VR + CT Virtual reality device: Joystim Number of sessions: 18 sessions Duration of sessions: 30 minutes Outcome measure: FMA+BBT Time since the onset of stroke: 6 or plus months	VR combined real instrument training was effective at promoting recovery of patients' upper extremity

2019/Nahid Norouzi-Gheidari	Feasibility, Safety and efficacy of a Virtual Reality Exergame System to Supplement Upper Extremity Rehabilitation Post-Stroke: A Pilot Randomized Clinical Trial and Proof of Principle	10.3390/ijerph17010113	18	Intervention group: VR + CT Virtual reality device: The Jintronix system Number of sessions: 4 weeks with the intervention group having 2 extra sessions per week. Duration of sessions: 30 minutes Outcome measure: FMA+BBT Time since the onset of stroke: no reference	Using virtual reality exergaming technology as an adjunct to traditional therapy is feasible and safe in post-stroke rehabilitation and may be beneficial to upper extremity functional recovery.
2018/Yoon-Hee Choi	Mobile Game-based Virtual Reality Program for Upper Extremity Stroke Rehabilitation.	10.3791/56241	24	Intervention group: VR + CT Virtual reality device: Mobile game Number of sessions: 10 sessions Duration of sessions: 60 minutes Outcome measure: FMA. Time since the onset of stroke: no reference	The findings of the present study suggest that this mobile game-based VR upper extremity rehabilitation program can be a substitute for some parts of conventional therapy that are delivered one-on-one by an occupational therapist.
2016/ Yoon-Hee Choi	Mobile game-based virtual reality rehabilitation program for upper limb dysfunction after ischemic stroke	10.3233/RNN-150626	24	Intervention group: VR + CT Virtual reality device: Mobile game Number of sessions: 10 sessions Duration of sessions: 60 minutes Outcome measure: FMA. Time since the onset of stroke: no reference	This mobile game-based VR rehabilitation program appears to be feasible and effective for promoting upper limb recovery after ischemic stroke.

2014/Pawel Kiper	Reinforced Feedback in Virtual Environment for Rehabilitation of Upper Extremity Dysfunction after Stroke: Preliminary Data from a Randomized Controlled Trial	10.1155/2014/752128	44	Intervention group: VR + CT Virtual reality device: PC workstation connected to a 3D motion tracking system and a high-resolution LCD projector displaying the virtual scenarios on a large wall screen. Number of sessions: 20 sessions Duration of sessions: 120 minutes Outcome measure: FMA+FIM Time since the onset of stroke: no reference	These results indicated that some poststroke patients may benefit from RFVE program for the recovery of upper limb motor function
2011/Mónica da Silva Cameirão	Virtual reality-based rehabilitation speeds up functional recovery of the upper extremities after stroke: A randomized controlled pilot study in the acute phase of stroke using the Rehabilitation Gaming System	10.3233/RNN-2011-0599	19	Intervention group: VR + CT Virtual reality device: The main elements of the Rehabilitation Gaming System (RGS) (Fig. 1) are: the vision-based Analysis and Tracking System (AnTS) Number of sessions: 20 sessions Duration of sessions: 35 minutes Outcome measure: Barthel index Time since the onset of stroke: 1 year	Our results suggest that rehabilitation with the RGS facilitates the functional recovery of the upper extremities. and that this system is therefore a promising tool for stroke neurorehabilitation.
2014/Chan Wai Yin	Virtual reality for upper extremity rehabilitation in early stroke: a pilot randomized controlled trial	10.1177/0269215514532851	23	Intervention group: VR + CT Virtual reality device: hand-held remote controller detected with a base movement sensor. Number of sessions: 10 sessions	Although additional VR training was not superior to conventional therapy alone, this study demonstrates the feasibility of VR training in early stroke.

				Duration of sessions: 30 minutes Outcome measure: FMA Time since the onset of stroke: no reference	
2018/Pawel Kiper	Virtual reality for upper limb rehabilitation in sub-acute and chronic stroke: a randomized controlled trial	10.1016/j.apmr.2018.01.023	136	Intervention group: VR + CT Virtual reality device: hand-held remote controller detected with a base movement sensor. Number of sessions: 20 sessions Duration of sessions: 120 minutes Outcome measure: FMA+FIM Time since the onset of stroke: maximum os 12 months after the stroke	The RFVE therapy combined with CR treatment promotes better outcomes for upper limb than the same amount of CR, regardless of stroke etiology.
2012/JH Crosbie	Virtual reality in the rehabilitation of the arm after hemiplegic stroke: a randomized controlled pilot study.	10.1177/0269215511434575	18	Intervention group: VR Virtual reality device: The system comprised a desktop computer, a head-mounted display unit, a motion tracking system and sensors. Number of sessions: 9 sessions Duration of sessions:30/45minutes Outcome measure: ARAT Time since the onset of stroke: maximum os 12 months after the stroke	A randomized controlled trial of virtual reality-mediated therapy comparable to conventional therapy would be feasible, with some suggested improvements in recruitment and outcome measures.

2018/Sevgi Ikbali Afsar	Virtual Reality in Upper Extremity Rehabilitation of Stroke Patients. A Randomized Controlled Trial	10.1016/j.jstrokecerebrovasdis.2018.08.007	42	Intervention group: VR Virtual reality device: Xbox Kinect system Number of sessions: 20 sessions Duration of sessions: 60 minutes Outcome measure: FMA+BBT Time since the onset of stroke: maximum os 12 months after the stroke	We found evidence that Kinect-base game system in addition to conventional therapy may have supplemental benefit for stroke patients
2017/Iris Brunner,	Virtual Reality Training for Upper Extremity in Subacute Stroke (VIRTUES)	10.1212/WNL.0000000000004744	120	Intervention group: VR + CT Virtual reality device: YouGrabber system Number of sessions: 20 sessions Duration of sessions: 60 minutes Outcome measure: ARAT Time since the onset of stroke: maximum of 12 weeks after the stroke	Additional upper extremity VR training was not superior but equally as effective as additional CT in the subacute phase after stroke.
2015/Nildo Manoel da Silva Ribeiro	Virtual rehabilitation via Nintendo Wii and conventional physical therapy effectively treat post-stroke hemiparetic patients	10.1179/1074935714Z.0000000017	30	Intervention group: VR Virtual reality device: Nintendo Wii Number of sessions: 16 sessions Duration of sessions: 60 minutes Outcome measure: FMA Time since the onset of stroke: maximum of 12 weeks after the stroke	Virtual rehabilitation using the Nintendo Wii and CPT both effectively treat post-stroke hemiparetic patients

2014/Kelly O Thielbar	Training finger individuation with a mechatronic-virtual reality system leads to improved fine motor control post-stroke	10.1186/1743-0003-11-171	14	Intervention group: VR Virtual reality device: actuated virtual keypad (AVK) system. Number of sessions: 18 sessions Duration of sessions: 60 minutes Outcome measure: FMA+ARAT Time since the onset of stroke: No reference.	Actively assisted individuation therapy comprised of non-task-specific modalities, such as can be achieved with virtual platforms like the AVK described here, may prove to be valuable clinical tools for increasing the effectiveness and efficiency of therapy following stroke.

The following bar chart shows the type of intervention applied to the intervention group. In the 26 trials analyzed, 16 had the intervention group doing VR based rehabilitation and CT, meanwhile the other 10 only used VR based rehabilitation.

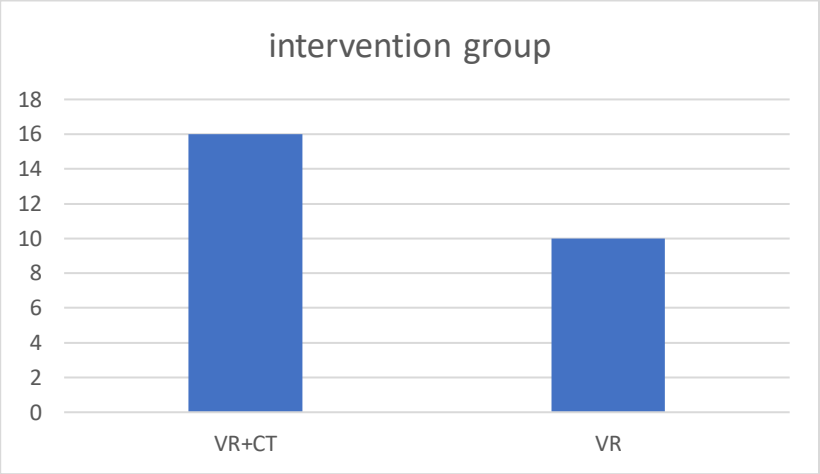

Figure 2- Bar chart of the intervention group.

The following bar chart shows the distribution of the number of sessions among the intervention group and control group of the 26 studies. In 3 of the 26 studies the intervention group had more sessions comparing with the control group.

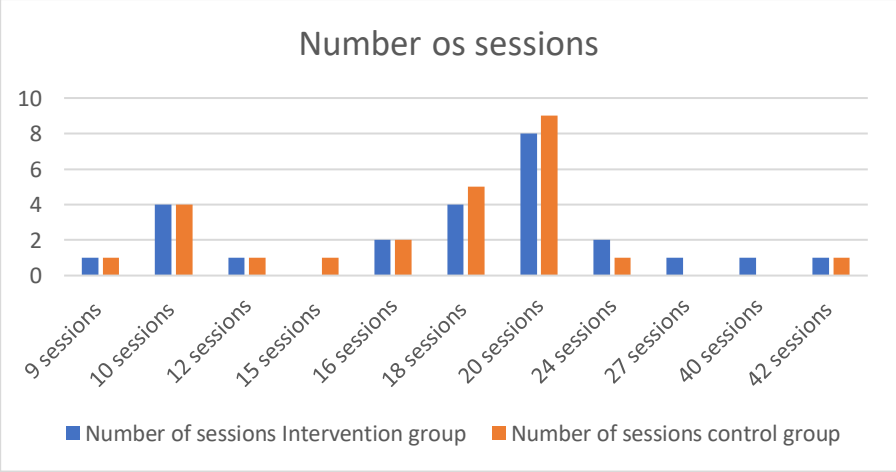

Figure 3 - Bar chart with all the different number of sessions in both intervention and control group.

The following bar chart shows the distribution of the duration of the sessions among the 26 trials. 60 minutes was prevalent time chosen for the session's duration.

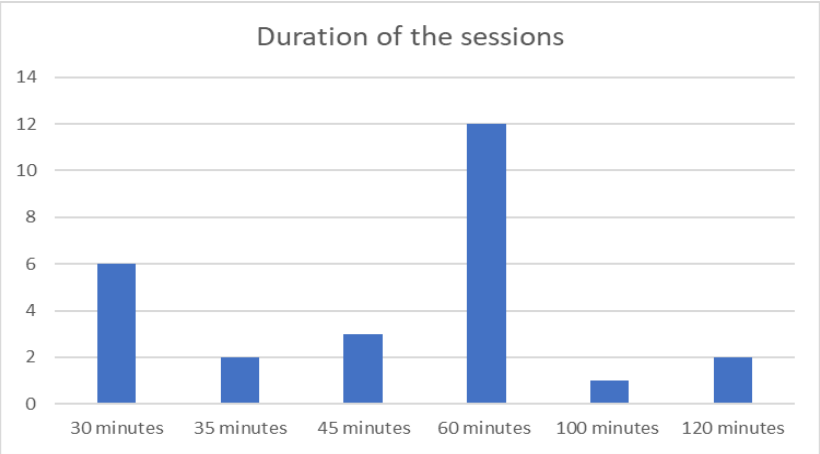

Figure 4 - Bar Chart of the durations of the sessions.

The following bar chart shows the used instruments for the VR based rehabilitation. There was a huge variety of devices used, but Xbox and Nintendo Wii were the most popular, being used in 4 trials each.

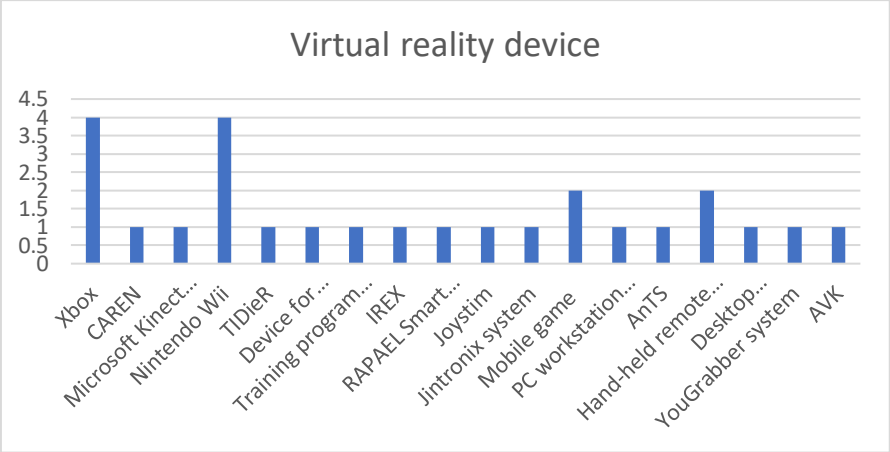

Figure 5 - Bar chart of the tool used in the intervention.

The following bar chart shows the distribution of the used scales to assess the outcomes of the trials. Some trials used more than one scale to measure outcomes and the most used scale was the FMA.

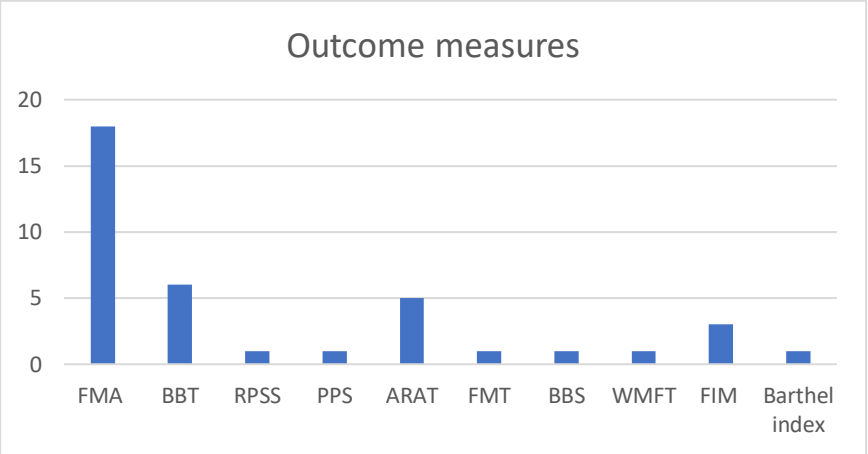

Figure 6 - Bar chart of the outcome measure scales used in the different trials.

The following bar chart shows the time since the onset of the stroke. Out of the 26 trials, 10 of them had no reference. Of the articles with reference to this information 6 months after stroke was the most prevalent with 6 trials.

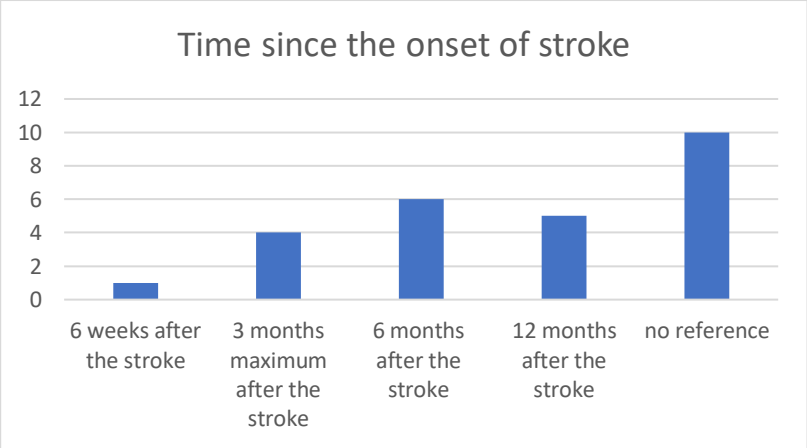

Figure 7 - Bar chart showing the time since the onset of the stroke.

DISCUSSION

The disabilities caused by a stroke can be life changing, impacting the personal and professional life of the patient in many ways, so rehabilitation plays a crucial role in the recovery and well-being of this people. This Master thesis aims to understand if there is a benefit in using the newer technologies in the form of Virtual Reality, for the rehabilitation of the upper limb in subjects who suffered a stroke. In total of 129 articles, only 25 of them met the quality and inclusion criteria.

Although this area is getting more and more attention in the last decade, we can still see that the studies that have been done have some negative points that should be address in other to achieve a greater scientific evidence.

With the 26 trials analyzed, there was a total of 1382 individuals involved, taking part of this narrative review. The 26 trials were evaluated using the Delphi list for the quality assessment of randomized control trials, in which the highest score was 7, with an average score of 6 with a variation of (+/-0.8) and a minimum score of 5, according to the quality scale. Among some weak points mentioned by the trials, the size of the sample was one with particular importance, with trials claiming that in order to have a more scientific relevance, the sample should be bigger.

Another problem we faced in making conclusion were the number of variables between the 26 articles. First, the type of intervention given to the intervention group, in which 16 out of the 26 intervention groups received a combination of VR plus CT (11,18,19,20,21,22,23,24,25,26,27,28,29,30,31,34). Another variable was the tool of VR used by the intervention group. In this variable there was a bigger pool of devices used but Xbox Kinect (11,18,20,33) and Nintendo Wii (14,22,23,35) were the most used with a total of 4 trials for each.

The number of sessions as well was different among the trials, and in this variable, in some trials the intervention group received more sessions than the control group. 20 sessions were the most choose number for the control group with 9 and for the intervention group with 8 (18,19,20,21,28,29,31,33,34). When it comes to the

duration of the sessions, 60 minutes were by far the most used amount of time with 12 out of the 26 trials choosing it (11,16,18,20,22,23,25,26,32,33,34,35).

Outcome measure was another variable with different scales being chosen, although FMA was by far the most used scale with a total of 18 (11,12,16,18,19,20,21,23,24,25,26,27,28,30,31,33,35,36).

Finally, the last variable was the time since the onset of the stroke, unfortunately in the variable not having reference to it was predominant with 10 trials (12,13,15,16,17,25,26,28,30,36).

CONCLUSIONS

The use of VR is a resource for the treatment of motor impairments of stroke and as mentioned above the constant innovation that we see nowadays must be used also in the medical area, but in order to be able to have a stronger evidence, that benefits the science and the patient, some changes must be done in order to lower the number of variables in play. Due to the number of variables in play, as I mentioned in the discussion, it is not possible to assume some actual connections between intervention and benefit for the patient, this way, future trials must standardize for some of these variables in to have crystal-clear scientific evidence, that then can be used for the benefit of the patients.

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ATTACHMENTS

Attachment 1 - List of Excluded Studies.

Title	Authors	DOI	Justification	Complementary Information
Benefits of virtual reality based cognitive rehabilitation through simulated activities of daily living: a randomized controlled trial with stroke patients.	Faria AL	10.1186/s12984-016-0204-z	Not aimed at the upper limb motor function	Focus on cognitive rehabilitation.
Virtual Reality Rehabilitation Versus Conventional Physical Therapy for Improving Balance and Gait in Parkinson's Disease Patients: A Randomized Controlled Trial.	Feng H	10.12659/MSM.916455	Not aimed at the upper limb motor function	Focus on gait and balance
Virtual Reality Reflection Therapy Improves Balance and Gait in Patients with Chronic Stroke: Randomized Controlled Trials.	In T	10.12659/msm.898157	Not aimed at the upper limb motor function	Focus on gait and balance
Virtual Reality Rehabilitation with Functional Electrical Stimulation Improves Upper Extremity Function in Patients with Chronic Stroke: A Pilot Randomized Controlled Study	Lee SH	10.1016/j.apmr.2018.01.030	Not aimed at VR study	Intervention is based on functional electrical stimulation

Effectiveness of Wii-based rehabilitation in stroke: A randomized controlled study.	Karasu AU	10.2340/16501977-2331	Not aimed at the upper limb motor function	Focus on balance
Elements virtual rehabilitation improves motor, cognitive, and functional outcomes in adult stroke: evidence from a randomized controlled pilot study.	Rogers JM	10.1186/s12984-019-0531-y	Not aimed at the upper limb motor function	
Does the addition of virtual reality training to a standard program of inpatient rehabilitation improve sitting balance ability and function after stroke? Protocol for a single-blind randomized controlled trial.	Sheehy L	10.1186/s12883-016-0563-x	Not aimed at the upper limb motor function	Focus on balance
Early post-stroke rehabilitation for upper limb motor function using virtual reality and exoskeleton: equally efficient in older patients.	Gueye T	10.5603/PJNNS.a2020.0096	No open access	
Maximizing post-stroke upper limb rehabilitation using a novel telerehabilitation interactive virtual reality system in the patient's home: study protocol of a randomized clinical trial.	Kairy D	10.1016/j.cct.2015.12.006	Study protocol	Study missing results

A low-cost virtual reality system for home based rehabilitation of the arm following stroke: a randomised controlled feasibility trial.	Standen PJ	10.1177/0269215516640320	Not aimed at studying stroke rehabilitation.	Study focusses on the feasibility, of a low-cost home-based rehabilitation.
Effectiveness of Early Rehabilitation Combined with Virtual Reality Training on Muscle Strength, Mood State, and Functional Status in Patients With Acute Stroke: A Randomized Controlled Trial.	Lin RC	10.1111/wvn.12429	Not aimed at the upper limb motor function	Focus on mood state and functional status
Home-based Upper Extremity Stroke Therapy Using a Multiuser Virtual Reality Environment: A Randomized Trial.	Thielbar KO	10.1016/j.apmr.2019.10.182	No open access	
Can robotic gait rehabilitation plus Virtual Reality affect cognitive and behavioural outcomes in patients with chronic stroke? A randomized controlled trial involving three different protocols.	Manuli A	10.1016/j.jstrokecerebrovasdis.2020.104994	Not aimed at the upper limb motor function	Focus on gait
Game-Based Virtual Reality Canoe Paddling Training to Improve Postural Balance and Upper Extremity Function: A Preliminary Randomized Controlled Study of 30 Patients with Subacute Stroke.	Lee MM	10.12659/MSM.906451	Not aimed at the upper limb motor function	Focus on postural balance

Virtual reality exercise improves mobility after stroke: an inpatient randomized controlled trial.	McEwen D	10.1161/STROKEAHA.114.005362	Not aimed at the upper limb motor function	Focus on mobility
Virtual-reality balance training with a video-game system improves dynamic balance in chronic stroke patients.	Cho KH	10.1620/tjem.228.69	Not aimed at the upper limb motor function	Focus on balance
Effectiveness, usability, and cost-benefit of a virtual reality-based telerehabilitation program for balance recovery after stroke: a randomized controlled trial.	Lloréns R	10.1016/j.apmr.2014.10.019	Not aimed at the upper limb motor function	Focus on balance
Virtual reality to augment robot-assisted gait training in non-ambulatory patients with a subacute stroke: a pilot randomized controlled trial.	Bergmann J	10.23736/S1973-9087.17.04735-9	Not aimed at the upper limb motor function	Focus on gait
Effects of virtual reality immersive training with computerized cognitive training on cognitive function and activities of daily living performance in patients with acute stage stroke: A preliminary randomized controlled trial.	Cho DR	10.1097/MD.0000000000014752	Not aimed at the upper limb motor function	Focus on cognitive rehabilitation
Effectiveness of virtual reality using Wii gaming technology in stroke rehabilitation: a pilot randomized clinical trial and proof of principle	Saposnik G	10.1161/STROKEAHA.110.584979	Not aimed at stroke rehabilitation	Focus on the feasibility and safety of the intervention

The role of virtual reality in improving motor performance as revealed by EEG: a randomized clinical trial	Calabrò RS	10.1186/s12984-017-0268-4	Not aimed at the upper limb motor function	Focus on balance and gait
Therapeutic Effect of Virtual Reality on Post-Stroke Patients: Randomized Clinical Trial.	Pedreira da Fonseca E	10.1016/j.jstrokecerebrovasdis.2016.08.035	Not aimed at the upper limb motor function	Focus on balance and gait
The efficacy of interactive, motion capture-based rehabilitation on functional outcomes in an inpatient stroke population: a randomized controlled trial.	Cannell J	10.1177/0269215517720790	Not aimed at the upper limb motor function	Focus on balance
The effects of robot-assisted gait training using virtual reality and auditory stimulation on balance and gait abilities in persons with stroke.	Park J	10.3233/NRE-172415	Not aimed at the upper limb motor function	Focus on gait
Video Game Rehabilitation for Outpatient Stroke (VIGoROUS): protocol for a multi-center comparative effectiveness trial of in-home gamified constraint-induced movement therapy for rehabilitation of chronic upper extremity hemiparesis.	Gauthier LV	10.1186/s12883-017-0888-0	Study protocol	Study missing resuts
A low cost kinect-based virtual rehabilitation system for inpatient	Kim WS	10.1097/MD.0000000000011173	Comparing two different types of VR	Intervention group received a low-cost VR, meanwhile the

rehabilitation of the upper limb in patients with subacute stroke				control group received a sham VR.
Adaptive conjunctive cognitive training (ACCT) in virtual reality for chronic stroke patients: a randomized controlled pilot trial.	Maier M	10.1186/s12984-020-0652-3	Not aimed at the upper limb motor function	Focus on cognitive rehabilitation
The Effect of a Virtual Reality Game Intervention on Balance for Patients with Stroke: A Randomized Controlled Trial.	Games Health J	10.1089/g4h.2016.0109	Not aimed at the upper limb motor function	Focus on balance
Does motivation matter in upper-limb rehabilitation after stroke? ArmeoSenso-Reward: study protocol for a randomized controlled trial	Widmer M	10.1186/s13063-017-2328-2	Study protocol	Study missing results
An Innovative STRoke Interactive Virtual thErapy (STRIVE) Online Platform for Community-Dwelling Stroke Survivors: A Randomized Controlled Trial.	Johnson L	10.1016/j.apmr.2020.03.011	No open access	
The Xbox/Kinect use in poststroke rehabilitation settings: a systematic review	Xavier-Rocha	10.1590/0004-282X20200012	Not aimed at the upper limb motor function	Focus on balance
Effect of Leap Motion-based 3D Immersive Virtual Reality Usage on Upper Extremity Function in Ischemic Stroke Patients	ÖGÜN	10.1590/0004-282x20190129	Duplicated	

Use of client-centered virtual reality in rehabilitation after stroke: a feasibility study	Aramaki	10.1590/0004-282x20190103	Not aimed at the upper limb motor function	Focus on performance
Effects of virtual reality therapy on upper limb function after stroke and the role of neuroimaging as a predictor of a better response	Gonçalves	10.1590/0004-282x20180104	Not aimed at VR study	The role of neuroimaging plays an important role in this trial.
applicability of a motor rehabilitation system in stroke victims	Carneiro	10.1590/1980-5918.029.004.ao08	Not aimed at stroke rehabilitation	Focus on the applicability of the Ikapp system.
Effect of a rehabilitation program using virtual reality for balance and functionality of chronic stroke patients	Silva	10.1590/S1980-65742015000300003	Not aimed at the upper limb motor function	Focus on balance
Exploring perspectives from stroke survivors, carers and clinicians on virtual reality as a precursor to using telerehabilitation for spatial neglect post-stroke	Helen Morse	10.1101/2020.01.07.20016782	Not aimed at the upper limb motor function	Focus on spatial neglect treatment
Effects of the addition of transcranial direct current stimulation to virtual reality therapy after stroke: a pilot randomized controlled trial.	Viana RT	10.3233/NRE-141065	Not aimed at VR study	The intervention group received transcranial direct current stimulation.
Effect of combined low-frequency repetitive transcranial magnetic stimulation and virtual reality training on upper limb function in subacute stroke:	Zheng CJ	10.1007/s11596-015-1419-0	Not aimed at VR study	The intervention group received low-frequency repetitive transcranial magnetic stimulation.

a double-blind randomized controlled trail				
Improving balance skills in patients who had stroke through virtual reality treadmill training.	Yang S	10.1097/PHM.0b013e3182389fae	Not aimed at the upper limb motor function	Focus on balance
Is upper limb virtual reality training more intensive than conventional training for patients in the subacute phase after stroke? An analysis of treatment intensity and content.	Brunner I	10.1186/s12883-016-0740-y	Not aimed at stroke rehabilitation	The study aimed to compare the intensity of a VR rehabilitation with a conventional one.
Combination transcranial direct current stimulation and virtual reality therapy for upper extremity training in patients with subacute stroke.	Lee SJ	10.1016/j.apmr.2013.10.027	Not aimed at VR study	The intervention group received cathodal transcranial direct current stimulation.
Visual dynamics cues in learning complex physical interactions	Hasson CJ	10.1038/s41598-019-49637-5	Not aimed at the upper limb motor function	Focus on balance and gait
Augmented Dyadic Therapy Boosts Recovery of Language Function in Patients With Nonfluent Aphasia.	Grechuta K	10.1161/STROKEAHA.118.023729	Not aimed at the upper limb motor function	Study focusses on linguistic rehabilitation
Virtual walking training program using a real-world video recording for patients with chronic stroke: a pilot study	Cho KH	10.1097/PHM.0b013e31828cd5d3	Not aimed at the upper limb motor function	Focus on balance and gait
Eliciting upper extremity purposeful movements using video games: a	Rand D	10.1177/1545968314521008	Not aimed at the upper limb motor function	Focus on balance and gait

comparison with traditional therapy for stroke rehabilitation				
A Preliminary Study of Dual-Task Training Using Virtual Reality: Influence on Walking and Balance in Chronic Poststroke Survivors	Fishbein P	10.1016/j.jstrokecerebrovasdis.2019.104343	Not aimed at the upper limb motor function	Focus on balance and gait
Improvement in balance using a virtual reality-based stepping exercise: a randomized controlled trial involving individuals with chronic stroke.	Lloréns R	10.1177/0269215514543333	Not aimed at the upper limb motor function	Focus on balance
Effects of transcranial direct current stimulation with virtual reality on upper limb function in patients with ischemic stroke: a randomized controlled trial	Yao X	10.1186/s12984-020-00699-x	Not aimed at VR study	Intervention is based on functional electrical stimulation
Effects of virtual reality training on occupational performance and self-efficacy of patients with stroke: a randomized controlled trial	Long Y	10.1186/s12984-020-00783-2	Not aimed at the upper limb motor function	Focus on performance status
Home-based hand rehabilitation after chronic stroke: Randomized, controlled single-blind trial comparing the MusicGlove with a conventional exercise program	Zondervan DK	10.1682/JRRD.2015.04.0057	No open access	
Innovative STRoke Interactive Virtual thErapy (STRIVE) online platform for	Johnson L	10.1136/bmjopen-2017-018388	Study protocol	Study without results

community-dwelling stroke survivors: a randomised controlled trial protocol.				
Cognitive-motor exergaming for reducing fall risk in people with chronic stroke: A randomized controlled trial.	Kannan L	10.3233/NRE-182683	Not aimed at the upper limb motor function	Focus on balance and cognitive rehabilitation
Virtual Reality Training with Cognitive Load Improves Walking Function in Chronic Stroke Patients.	Cho KH	10.1620/tjem.236.273	Not aimed at the upper limb motor function	Focus on balance and cognitive rehabilitation
High Frequency and Intensity Rehabilitation in 641 Subacute Ischemic Stroke Patients	Tollár J	10.1016/j.apmr.2020.07.012	Not aimed at the upper limb motor function	Focus on balance and gait
Effectiveness of Virtual Reality Exercises in STroke Rehabilitation (EVREST): rationale, design, and protocol of a pilot randomized clinical trial assessing the Wii gaming system.	Int J	10.1111/j.1747-4949.2009.00404	Study protocol	Study without results
Stroke Rehabilitation with Distorted Vision Perceived as Forces	Hajissa E	10.1109/ICORR.2019.8779410	No open access	
Cost-analysis of virtual reality training based on the Virtual Reality for Upper Extremity in Subacute stroke (VIRTUES) trial	Islam MK	10.1017/S026646231900059X	Not aimed at stroke rehabilitation.	Study focused on the cost analysis a specific VR training
A comparison of two personalization and adaptive cognitive rehabilitation	Faria AL	10.1186/s12984-020-00691-5	Not aimed at the upper limb motor function	Focus on cognitive rehabilitation

approaches: a randomized controlled trial with chronic stroke patients				
Toward Improving Poststroke Aphasia: A Pilot Study on the Growing Use of Telerehabilitation for the Continuity of Care.	Maresca G	10.1016/j.jstrokecerebrovasdis.2019.104303	Not aimed at the upper limb motor function	Focus on linguistic rehabilitation
Virtual reality training for upper extremity in subacute stroke (VIRTUES): study protocol for a randomized controlled multicenter trial.	Brunner I	10.1186/s12883-014-0186-z	Study protocol	Study without results
A task-specific interactive game-based virtual reality rehabilitation system for patients with stroke: a usability test and two clinical experiments	Shin JH	10.1186/1743-0003-11-32	Not aimed at stroke rehabilitation	Study focusses on improving a specific VR tool.
Counteracting learned non-use in chronic stroke patients with reinforcement-induced movement therapy.	Ballester BR	10.1186/s12984-016-0178-x	Comparing two different types of VR	Both control and intervention group received VR-based rehabilitation
Combining levodopa and virtual reality-based therapy for rehabilitation of the upper limb after acute stroke: pilot study Part II.	Samuel GS	10.11622/smedj.2016111	Not aimed at VR study	The intervention group had levodopa neuromodulation
Using mixed methods to evaluate efficacy and user expectations of a virtual reality-based training system for	Schuster-Amft C	10.1186/1745-6215-15-350	No open access	

upper-limb recovery in patients after stroke: a study protocol for a randomised controlled trial.				
Neural reorganization accompanying upper limb motor rehabilitation from stroke with virtual reality-based gesture therapy	Orihuela-Espina F	10.1310/tsr2003-197	No control group	
Patients' use of a home-based virtual reality system to provide rehabilitation of the upper limb following stroke	Standen PJ	10.2522/ptj.20130564	Not aimed at stroke rehabilitation	Study focusses on the adherence to the home-based VR system
Effects of game-based virtual reality on health-related quality of life in chronic stroke patients: A randomized, controlled study.	Shin JH	10.1016/j.compbiomed.2015.03.011	Not aimed at the upper limb motor function	Focus on the quality of life and depression
Asymmetric training using virtual reality reflection equipment and the enhancement of upper limb function in stroke patients: a randomized controlled trial.	Lee D	10.1016/j.jstrokecerebrovasdis.2013.11.006	No open access	
Prospective clinical study of rehabilitation interventions with multisensory interactive training in patients with cerebral infarction: study protocol for a randomised controlled trial.	Lo WL	10.1186/s13063-017-1874-y	Study protocol	

Effects of virtual reality training on gait biomechanics of individuals post-stroke.	Mirelman A	10.1016/j.gaitpost.2010.01.016	Not aimed at the upper limb motor function	Focus on gait
A randomised trial of social support group intervention for people with aphasia: A Novel application of virtual reality.	Marshall J	10.1371/journal.pone.0239715	Not aimed at the upper limb motor function	Focus on wellbeing, communication and quality of life
Experience of an upper limb training program with a non-immersive virtual reality system in patients after stroke: a qualitative study	Lehmann I	10.1016/j.physio.2017.03.001	Not aimed at stroke rehabilitation	Focused on the feedback and expectations from the intervention