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Summary

Most domains of conventional rehabilitation programs suffer from high costs, demand constraints, difficult to access, time consuming, and mundane repetition that bores patients, resulting in low patient adherence to prescribed regimens. The interest in AR and VR technologies, thus, can be primarily attributed to deal with the limitations present in conventional rehabilitation programs, namely that such technologies are easily accessible, easy to use, and a cost effectiveness solution in the long run.

This paper gives an overview of the current researched techniques of AR and VR technologies in medical rehabilitation. The overview includes a variety of medical application domains, with patient conditions ranging from burns and injuries up to chronic conditions such as stroke. The techniques discussed in this paper are all recent developments, with no technique cited being from the early 2010's. This is to ensure that the technologies used are up-to date and representative of the most advanced developments so far.

The techniques discussed vary in multiple ways, such as their setups, hardware, intervention, duration, target patients to name a few. Most of the papers reviewed con- firmed the benefits of AR and VR in medical rehabilitation, especially those of continued patient motivation and engagement. Benefits related to therapy outcomes varied depending on factors such as the illness, intervention, duration, etc. Some reported a significant improvement in outcomes of AR and VR interventions, whereas others reported no significant differences in outcome between conventional approach and AR/VR fortified interventions. However, it is worth noting that many of the discussed interventions studied AR and VR usage *in-addition* to prescribed ongoing conventional therapy, so the current findings can only confirm their efficiency and effectiveness as an adjunct to conventional therapy, and not a stand-alone treatment.

Περίληψη

Οι περισσότεροι τομείς των συμβατικών προγραμμάτων αποκατάστασης μαστίζονται από υψηλό κόστος, προβλήματα ζήτησης, δύσκολη πρόσβαση, χρονοβόρα και συνεχή επανάληψη που προκαλεί δυσανασχέτηση στους ασθενείς, με αποτέλεσμα τη χαμηλή συμμόρφωση των ασθενών σε συνταγογραφούμενα σχήματα. Το ενδιαφέρον για τις τεχνολογίες AR και VR, επομένως, μπορεί να αποδοθεί κυρίως στην αντιμετώπιση των περιορισμών που υπάρχουν στα προγράμματα συμβατικής αποκατάστασης, δηλαδή ότι τέτοιες τεχνολογίες είναι εύκολα προσβάσιμες, εύχρηστες και μια λύση αποδοτικότητας κόστους μακροπρόθεσμα.

Αυτή η εργασία δίνει μια επισκόπηση των τρεχουσών ερευνητικών τεχνικών των τεχνολογιών AR και VR στην ιατρική αποκατάσταση. Η επισκόπηση περιλαμβάνει μια ποικιλία τομέων ιατρικών εφαρμογών, με παθήσεις ασθενών που κυμαίνονται από εγκαύματα και τραυματισμούς έως χρόνιες παθήσεις όπως εγκεφαλικό επεισόδιο. Οι τεχνικές που εξετάζονται σε αυτή την εργασία είναι όλες πρόσφατες εξελίξεις, χωρίς καμία τεχνική να αναφέρεται από τις αρχές της δεκαετίας του 2010. Αυτό γίνεται για να διασφαλιστεί ότι οι τεχνολογίες που παρουσιάζονται είναι ενημερωμένες και αντιπροσωπευτικές των πιο προηγμένων εξελίξεων μέχρι στιγμής.

Οι τεχνικές που συζητήθηκαν ποικίλλουν με πολλούς τρόπους, όπως οι ρυθμίσεις, τα υλικά, η παρέμβαση, η διάρκεια, η στόχευση των ασθενών, για να αναφέρουμε μερικούς. Οι περισσότερες από τις εργασίες που εξετάστηκαν επιβεβαίωσαν τα οφέλη της AR και της VR στην ιατρική αποκατάσταση, ειδικά εκείνα της συνεχούς κινητοποίησης και εμπλοκής των ασθενών. Τα οφέλη που σχετίζονται με τα αποτελέσματα της θεραπείας ποικίλλουν ανάλογα με παράγοντες όπως η ασθένεια, η παρέμβαση, η διάρκεια κ.λπ. Ορισμένοι ερευνητές ανέφεραν σημαντική βελτίωση στα αποτελέσματα των παρεμβάσεων AR και VR, ενώ άλλοι δεν ανέφεραν σημαντικές διαφορές στο αποτέλεσμα μεταξύ της συμβατικής προσέγγισης και των ενισχυμένων επεμβάσεων AR/VR. Ωστόσο, αξίζει να σημειωθεί ότι πολλές από τις παρεμβάσεις που συζητήθηκαν μελέτησαν τη χρήση AR και VR εκτός από τη συνταγογραφούμενη συνεχιζόμενη συμβατική θεραπεία, οπότε τα τρέχοντα ευρήματα μπορούν μόνο να επιβεβαιώσουν την συνολική

αποτελεσματικότητα τους ως συμπλήρωμα της συμβατικής θεραπείας, και δεν αποτελεί μια αυτόνομη θεραπευτική τακτική.

Αντικείμενο της διπλωματικής εργασίας

Αντικείμενο της διπλωματικής εργασίας είναι η επισκόπηση των τρεχουσών ερευνητικών τεχνικών των τεχνολογιών AR και VR στην ιατρική αποκατάσταση. Η επισκόπηση περιλαμβάνει μια ποικιλία τομέων ιατρικών εφαρμογών, με παθήσεις ασθενών που κυμαίνονται από εγκαύματα και τραυματισμούς έως χρόνιες παθήσεις όπως εγκεφαλικό επεισόδιο. Οι τεχνικές που εξετάζονται σε αυτή την εργασία είναι όλες πρόσφατες εξελίξεις, χωρίς καμία τεχνική να αναφέρεται από τις αρχές της δεκαετίας του 2010. Αυτό γίνεται για να διασφαλιστεί ότι οι τεχνολογίες που παρουσιάζονται είναι ενημερωμένες και αντιπροσωπευτικές των πιο προηγμένων εξελίξεων μέχρι στιγμής.

1 Introduction

1.1 Defining Rehabilitation

1.1.1 What is Rehabilitation?

Rehabilitation is care that can help patients get back, keep, or improve abilities that are needed for daily life. These abilities may be physical, mental, and/or cognitive (thinking and learning). Rehabilitation is a multifaceted long-term process ranging from inpatient or outpatient rehabilitation up to subsequent rehabilitation services. When a patient gets rehabilitation, they often have a team of different health care providers helping them. They will work with the patient to figure out their needs, goals, and treatment plan. The types of treatments that may be in a treatment plan include:

- Assistive devices, which are tools, equipment, and products that help people with disabilities move and function,
- Cognitive rehabilitation therapy to help relearn or improve skills such as thinking, learning, memory, planning, and decision making,
- Mental health counseling,
- Music or art therapy to help express your feelings, improve your thinking, and develop social connections,
- Nutritional counseling,
- Occupational therapy to help with daily activities,
- Physical therapy to help strength, mobility, and fitness,
- Recreational therapy to improve your emotional well-being through arts and crafts, games, relaxation training, and animal-assisted therapy,
- Speech-language therapy to help with speaking, understanding, reading, writing, and swallowing,
- Treatment for pain,
- Vocational rehabilitation to help build skills for going to school or working at a job.

Depending on the patients' needs, they may have rehabilitation in the providers' offices, a hospital, or an inpatient rehabilitation center. In some cases, a provider may come to their home. If they do get care at home, they commonly will need to have family members or friends who can come and help with the rehabilitation. [1]

1.1.2 Who Needs Rehabilitation?

Rehabilitation is for people who have lost abilities that they need for daily life. Some of the most common causes include:

- Injuries and trauma, including burns, fractures (broken bones), traumatic brain injury, and spinal cord injuries,

- Stroke,
- Severe infections,
- Major surgery,
- Side effects from medical treatments, such as from cancer treatments,
- Certain birth defects and genetic disorders,
- Developmental disabilities,
- Chronic pain, including back and neck pain.

The overall goal of rehabilitation is to help the patient get their abilities back and regain independence. But the specific goals are different for each person. They depend on what caused the problem, whether the cause is ongoing or temporary, which abilities you lost, and how severe the problem is. For example, a person who has had a stroke may need rehabilitation to be able to dress or bathe without help, or an active person who has had a heart attack may go through cardiac rehabilitation to try to return to exercising, or someone with a lung disease may get pulmonary rehabilitation to be able to breathe better and improve their quality of life. [1]

1.1.3 Principles of Rehabilitation

The principles of neurorehabilitation to elicit motor learning and brain plasticity include repetitive mass practice, practice dosage, task-oriented and goal-specific functional training, randomized variable practice, multisensory stimulation, and increasing difficulty [2]. To maintain the success of rehabilitation, an ongoing execution of acquired changes and a long-term provision of subsequent rehabilitation services are required [3].

1.1.4 Limitations in Conventional Modes of Rehabilitation Therapies

Current modes of therapies available for patients have several limitations and hurdles. These methods are becoming more and more unsustainable as they usually require one-on-one patient-practitioner sessions, which induce high costs, require dedicated time and space, and are subject to availability. The simple and repetitive exercises is also a hurdle, as it induces boredom in the patients, which reduces their motivation [4]. Furthermore, treatment data are not collected because simple exercising devices are designed with no sensors. Home-based technologies have been proposed to help patients to conduct rehabilitation at home. Without any technical support home sessions must be easily understood and performed by patients. This often leads to the implementation of simple sets of repetitive exercises. For such interventions, the motivation of the patient to perform the exercises is of the utmost importance. Long term rehabilitation might not be achieved due to lack of patients' adherence. However, there is strong evidence that these limitations can be mitigated by a more entertaining, engaging, and enjoyable form of delivering therapy exercises.

Another one of the major limitations of conventional rehabilitation programs is an inadequate dose of rehabilitation therapy, in terms of repetition and intensity. Patients often receive insufficient rehabilitation therapy after an acquired neurological condition [5]. For instance, the current evidence suggests that there is a high practice threshold required to achieve significant upper-limb functional improvements [6]; this threshold is achievable in humans [7] to deliver the repetition and intensity that are thought to be important in experience-dependent plasticity [8]. Pollock et al. found moderate quality evidence of benefit from a high dose of task practice but not for a low dose [9]. There is hope that new approaches to rehabilitation could increase the therapy dose.

Patient adherence to prescribed in-home rehabilitative regimens has significant im- pacts on recovery time and overall patient outcomes [10,11]. Prior studies have identified several factors influencing patient adherence, primarily social/family support, time, space, and motivation [12]. Patient self-motivation and self-efficacy are crucial to adherence, as are features of the regimen that support patients to feel competent [11].

1.2 Rehabilitation Technologies

The idea of rehabilitation carried out with the help of digital technologies is gaining traction and interest over the recent years, and the present-day mass-market adoption of the immersive technology brought new promise related to the application of such interfaces to patient rehabilitation. Rehabilitation technologies are defined as "those whose primary purpose is to maintain or improve an individual’s functioning and independence, to facilitate participation and to enhance overall well-being" [13]. Rehabilitation technologies therefore overlap partially with robotics but also encompass non-robotic technologies, e.g. environmental control systems and communication devices. Rehabilitation technology development has been identified as a priority area for research by the Medical Rehabilitation Research Coordinating committee (USA) [5]. There are a wide range of technologies with applications in rehabilitation including robotic and virtual reality technologies, assistive devices, neuroprostheses and even smartphone applications [5].

1.2.1 Defining Augmented and Virtual Realities

Virtual Reality (VR) aims to create an environment that the users feel as realistic and coherent: they should experience “presence” - the illusion of “being there” in the simulated environment and the feeling that what is happening is plausible. Indeed, the simulated events must follow precise physical laws, satisfy psychosocial expectations, and synchronize with the user’s actions [14]. VR immerses the observer into a completely simulated virtual world and can be delivered by Head-Mounted Displays, Powerwall screens, or Cave Automatic Virtual Environments. More generally, VR can be defined as any computer-based device that provides visual stimuli on a monitor or wall screen display, like video games. These can be considered as less immersive virtual environments when compared to Head- Mounted Displays [15–17].

Augmented Reality (AR) aims to superimpose virtual information on the physical world, where computer-generated graphics are superimposed on a user’s view of the real world, providing him with more information about the objects he is seeing. Just like VR, AR should synchronize the virtual simulation with the real world to give a fair degree of realism and a sense of presence [18]. Since the virtual objects extend the real environment (the users “are already there”), the sense of presence in AR could be better defined as “informed continuity”. AR is usually provided through specific purpose glasses, called smart glasses (e.g., Microsoft Hololens, Epson MOVERIO), or any device with a screen and a camera, like a tablet or a smartphone [15].

The Reality-Virtuality Continuum as presented in Fig.1provides a classification scale of all possible variations between a completely virtual environment and a completely real environment. The area between the two extremes is called Mixed Reality (MR) where both reality and virtuality are mixed under different conditions [19]. In MR, the observer is immersed in a mix of real and virtual objects that interact with each other by adding certain virtual objects to the real world and filtering visual information about real objects from the real world.

The efficacy of both VR and AR lies, thus, in the creation of a coherent simulation: the users must experience the same physical laws during the whole simulation and perceive synchronicity between their (re)actions and the virtual stimuli. Once accustomed to the simulation, the users must see congruence between what is happening and their expectations [18]. If the simulated environment lacked coherence, users would feel it as non-realistic: they would live a poor experience, the simulation would fail to induce positive effects, and adverse effects such as cybersickness (i.e., the feeling of discomfort and malaise due to the mismatch between observed and expected sensory signals) could occur. Note that some forms of sickness, e.g., motion sickness, can occur even if users experience presence: in fact, for both presence and cybersickness to occur, the patients have to feel the simulation as realistic [18,21].

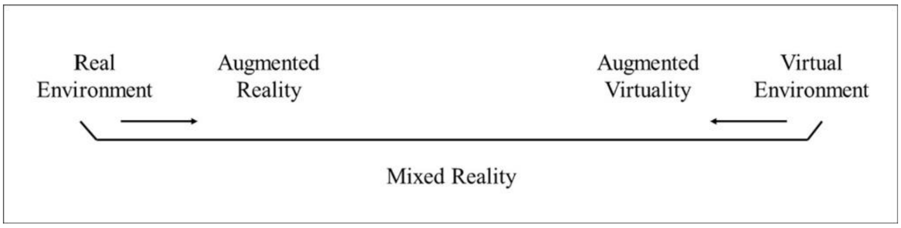


Figure 1: Reality-Virtuality Continuum [20]

1.2.2 Rise of Augmented and Virtual Reality in Rehabilitation

The application of VR and AR is gaining popularity and scholarly interest because of the possibility to generate environmental and perceptual stimuli [22], which transform the user experience offering high levels of "personal efficacy" (beliefs about own capability to accomplish challenging goals), and "self-reflectiveness" (intense focus on the particular instance or experience), generated by the user sense of presence and emotional engagement [23].

VR and AR have drawn professionals and patients’ attention in several fields, including psychology, physical, and neurological rehabilitation, and surgery. In particular, the development of low-cost head-mounted displays (HMDs), which can be associated with smartphones, gaming consoles, personal computers, or workstations, brought VR and AR outside research laboratories toward a vast audience of users [14,18]. VR and AR typically use input devices to gather information about the user (e.g., the position of the body and its kinetic information) and the surrounding environment, and output devices to send the user sensory information (e.g., images, vibrations, and sounds) [18].

In more recent years, Augmented Reality and Virtual Reality training systems combined with desktop computers and smartphone apps have been used as an adjunct to conventional rehabilitation. These technologies provide new opportunities to increase the feeling of immersion in interactive applications, which can be combined with other game development techniques to increase user engagement, ultimately resulting in an improved overall experience [16].

These technologies are becoming an increasingly researched topic for usage as rehabilitation therapeutic tools in the healthcare setting. These technologies reduce patient hospitalization times and costs and increase the number of patients who can be treated at the same time [24]. Another positive aspect of these rehabilitative modes is direct and continuous interaction between the patient and the health care provider, which increases compliance to treatment [25]. Studies demonstrated that remote virtual rehabilitation enhances patient’s motivation improving adherence to therapy [26], because in comparison to the conventional retraining techniques they offers an artificial environment where the training environment, difficulty level of tasks, and the feedback types could be relatively effortlessly manipulated [27].

2 Literature Review

2.1 Researched Domains of Application of AR/VR in Medical Rehabilitation

VR involves using interactive simulations produced by computer technology to allow users to engage in environments that closely resemble the real-world. In AR, the user can see the real world around him while virtual objects are additionally presented to the real world. The provision of visual and often multi-sensory feedback is a key attribute of these technologies. Both technologies can be used for simulated independent practice at higher doses than that could be achieved through conventional therapy [9].

These technologies have shown to improve static and dynamic balance, mobility, gait, stride length, sitting and standing time, fear of movements and risk of falls, aerobic and motor function, muscle tension and strength, and activities of daily life in various populations, healthy or with some disorder (e.g., balance deficit, spinal cord injuries, stroke, PD, and multiple sclerosis) [28–35]. VR also improves executive functions, driving attitude, attention, learning, and problem solving-skills in case of traumatic brain injury [36].

VR has also been shown to improve attention in people with unilateral spatial neglect (USN), a neurological disorder that commonly follows injuries (e.g., stroke) to one brain hemisphere and induces deficit in responding to stimuli placed on one side on the vision field [37]. VR helps reduce musculoskeletal related pain (e.g., chronic neck pain and shoulder impingement syndrome), although often similar or inferior to recommended exercises [38]. Other fields of immersive interfaces applications were rehabilitation in cerebral vascular accident (CVA) [39,40], cerebral palsy [41,42] and even rare diseases [43].

2.1.1 Hand Injuries

The human hand is the part of the body most frequently injured in work-related accidents, accounting for a third of all accidents at work and often involving surgery and long periods of rehabilitation. Several applications of Augmented Reality (AR) and Virtual Reality (VR) have been used to improve the rehabilitation process. Several disabilities as sequelae of injury can affect the hand and its motor control. The overall cost and the burden of these injuries to the patient can be very extensive, and its economic effect goes well beyond hospitalization cost, also including significant aftercare costs, lost productivity, and other intangible costs [44,45].

Rehabilitation usually takes the form of therapy sessions. In these sessions, patients perform specific exercises for a fixed period, under the supervision of a health professional, typically a physiotherapist or an occupational therapist. The main cost factor in these conventional therapies resides in scalability i.e., in the occupation of the required facilities and the full-time intervention of healthcare professionals in sessions, limiting the number of patients that can be treated at any given time.

Pereira et al. reviewed clinical studies for which AR/VR systems were developed and tested for hand rehabilitation in several different pathologies and concluded that six showed improvements in the intervention group, compared to the conventional therapy group, and 2 showed no statistical difference between both groups. Although still consisting of studies with a small sample of participants, they all had a comparison between AR/VR rehabilitation and conventional therapy [20].

2.1.2 Parkinson’s Disease

Parkinson’s disease (PD) is a common neurodegenerative disease with progressive development. The pathological changes of the disease are degeneration of the substantia nigra and striatum pathway [46]. The clinical manifestations are motor symptoms such as bradykinesia, dystonia, tremor and postural balance disorder, and non-motor symptoms such as cognitive decline and depression [47]. Freezing of gait is also one of the common complications of PD patients, often occurring in the advanced stages of the disease. With this complication, despite the patient’s attempt to walk, the forward progression of the feet is significantly reduced, increasing the risk of falls, and creating difficulties in the patient’s care. Currently, drug therapy is the preferred treatment for PD, but it is effective only for the first years after onset and some symptoms do not respond at all to drug treatment.

Deep brain stimulation is one of the current treatments for primary PD where electrodes are implanted in the brain to stimulate the targeted area and improve the related symptoms of PD patients. However, improper intraoperative electrode positioning, or stimulation parameters may not only affect the therapeutic effect, but also stimulate the peripheral nerve conduction bundle, causing various types of motor, sensory symptoms and other adverse reactions [48]. It has been reported that long-term rehabilitation training can improve the motor ability and cognitive outcome of patients with PD. However, in actual clinical practice, long-term rehabilitation training has high requirements for the ability of rehabilitation therapists, the financial situation of patients, training places, and the safety of patients. As a result, it is difficult for people with PD to obtain and maintain long-term regular training.

One of the most promising treatments for patients with PD is VR [49], which can provide visual, auditory, and somatosensory stimuli to assist in improving gait for individuals with PD. From the perspective of kinematics learning, VR provides a possibility for high-intensity, task-oriented and multi-sensory feedback training, which can promote patients’ visual, auditory and tactile input, and increase their interest in the rehabilitation process by letting patients experience immersion or non-immersion virtual environment, so that patients’ treatment compliance is effectively improved [50,51]. Previous studies have confirmed that VR technology plays an active role in stroke [30], cognitive function and quality of life in the elderly [52]. It has also been shown that VR can improve the balance function and daily life activities of patients with PD [53].

VR enables people to interact with an artificial world, while health professionals can monitor and evaluate their progress. External stimuli are beneficial in improving gait in patients with PD [54], with an additional increase in speed associated with the use of visual cues [55]. VR can provide patients with more sensory stimulation, a more immersive environment, and real-time feedback during specific motor tasks [56], reflecting motor learning and neuroplasticity [57]. Therefore, this approach can be considered as a complement to traditional rehabilitation therapies.

Lei et al. [31] conducted a systematic review of VR rehabilitation training for PD patients and focused on the improvement of gait and balance. They found that VR rehabilitation training performed better than conventional or traditional rehabilitation training in step and stride length, balance function, and mobility. As for the secondary outcomes, it had similar effects on global motor function, activities of daily living, and cognitive function. They reported improved health-related quality of life (HRQoL), level of confidence in difficult activities that could cause falls, and neuropsychiatric symptoms (i.e., anxiety and depression) more than standard care, conventional therapy, or any other non-VR rehabilitation program for PD. Moreover, VR has been shown to reduce neuropathic pain in spinal cord injuries [31], anxiety, and depressive symptoms in people with PD [35].

de Amorim et al. [33] conducted a systemic review with the aim to summarize the effects of physical therapy interventions with VRT in the rehabilitation of balance in the elderly. They found evidence for improved static and dynamic balance, mobility, gait, and reduced sitting and standing time, fear, and risk of falls in various elderly samples, healthy or with some disorder (e.g., balance deficit, diabetes mellitus, or PD) more than placebo, standard proprioceptive training, and kinesiotherapy groups.

2.1.3 Spinal Cord Injury

Spinal cord injury (SCI) is a common neurological condition that often results in long-term impairments in physical function and psychological and socioeconomic status [58]. Because of functional limitations in the sensory and motor systems, which may involve both lower and upper limb functions, SCI drastically affects independence and quality of life [59]. Different types of training and stimulation protocols are commonly used to induce or facilitate processes of neural regeneration and plasticity, which might lead to significant functional recovery after SCI [60]. Therefore, appropriate rehabilitation strategies are highly needed to regain sensorimotor function and reduce symptoms such as spasticity, imbalance, and neuropathic pain.

Ahern et al. [34] conducted a systemic review and meta-analysis to investigate the effectiveness of VR technology in the management of individuals with acute, subacute, and chronic spinal pain. They reported reduced fear of movement in patients with low back pain (LBP) more than conventional stabilization exercises or physical therapy. Chi et al. [35] conducted a systemic review to investigate the effect of VR therapy on SCI-associated neuropathic pain. The included studies used VR therapy as virtual walking, VR-augmented training, virtual illusion, and VR hypnosis for treating neuropathic pain, and found that each VR method reduced neuropathic pain.

Araújo et al. conducted a systemic review to investigate the possible benefits and efficacy of VR-based rehabilitation in individuals with SCI [29]. VR-based interventions in patients with SCI demonstrated to improve motor function [61–63], neuropathic pain [61,64], balance [61,65,66], and aerobic function [67,68]. The level of engagement affects the degree of active participation which in turn can improve outcomes. Mekki et al. demonstrated that when individuals were given both feedback on their walking speed and competition against virtual opponents, there was increased muscle activity [69].

2.1.4 Pulmonary Disease

Based on the reports of the American Thoracic Society and the European-Respiratory Society, chronic obstructive pulmonary disease (COPD) is the third leading cause of mortality worldwide. COPD symptoms include not only shortness of breath, chronic cough, and sputum production, but also reduced exercise tolerance. Traditional programs of pulmonary rehabilitation have been shown to be capable of at least partially reversing muscle dysfunction and improving mobility; it is the most effective therapy to improve exercise tolerance in chronic respiratory diseases, idiopathic pulmonary fibrosis, and lung cancer. However, in international surveys, traditional pulmonary rehabilitation is available to only a small fraction of COPD patients. Alternate modes of rehabilitation are sought which might increase availability to patients who would benefit.

Rutkowski et al. conducted a randomized control trial on hospitalized patients who used a VR rehabilitation system. These patients showed improvement in physical fitness in all the Senior Fitness Test components. Hence, this study suggested that a pulmonary rehabilitation program supplemented with virtual rehabilitation training is a beneficial intervention for enhancing physical fitness in patients with COPD [70].

2.1.5 Stroke

Individuals who have survived neurological injuries such as a stroke often have sensory impairments, including in proprioception, and therefore have lost some of the normal feedback associated with a typical motor action [9]. Psychological problems are also common after stroke and SCI [71,72], and strategies that focus on patient engagement are important for successful rehabilitation [5]. Stroke is also one of the most common causes of disability and poor quality of life. In addition, it affects health and social care systems by poor performance at work, increased dependency, and demands on healthcare. Because the Upper Limbs (ULs) and Lower Limbs (LLs) are involved in most daily living activities, it is necessary to improve ULs and LLs' functional utilization after stroke.

Several studies have found that VR for stroke survivors has benefits over gym- based interventions for upper-limb function [73,74], balance and weight distribution [75], and motor control of the eyes, head, and neck [76]. VR has now been incorporated into varied clinical practices such as post-stroke rehabilitation, and it has shown significant effects on improving the motion functions, dynamic balance, and muscle force of both upper and lower limbs among stroke patients [77,78]. AR/VR can present visual stimulus and feedback that may support motor rehabilitation via activation of neurons in brain matter damaged by stroke events [73]. These benefits may generalize to other rehabilitative patients. Mirror neuron activation by visual stimulus in AR/VR may support internalization of competent execution of exercises.

Iruthayarajah et al. [30] conducted a systematic review and meta-analysis on the effectiveness of VR interventions for improving balance in a chronic stroke population. They reported improvements in aerobic and motor function, muscle tension, muscle strength, and activities of daily life alone or in combination with occupational therapy or physiotherapy. In addition to VR-based technologies, several systematic reviews have further confirmed the promising effects of AR in rehabilitation, especially for stroke patients [73, 79–83]. As such, AR/VR-guided rehabilitation proves to be effective in increasing motivation and adding excitement to rehabilitation practices, consequently leading to increased investment by the patients themselves. Similar results have been extensively studied in re- habilitation for stroke patients [78], results which remain highly applicable towards upper limb rehabilitation programs [84].

2.1.6 Amputee Rehabilitation - Prostheses

Due to the efforts within the field of prosthetics, amputees have been able to achieve higher degrees of motion and control aided with the development of myoelectric prosthetics. However, the functionality of these prosthetics remains limited, and coupled with the high rejection rate of these devices, development in the field has significant room for improvement. A common cause of prosthetic rejection is unsuccessful rehabilitation therapy, in which the amputee is unable to develop the sufficient skills needed to successfully manage their pros- thesis during Activities of Daily Living (ADLs) [85]. Some of the major problems leading to rehabilitation failure include the late start of post-traumatic intervention due to wait time for a prosthetic fit, a lack of objective assessment of the patient's progress and performance [86], and poor patient motivation to commit to the repetitive practices involved in rehabilitation [87].

AR/VR technologies have shown promising potential to ameliorate the rehabilitation process in prosthetics. By using a virtual arm instead of waiting for a prosthetic, patients can start rehabilitation immediately after trauma, consequently reducing the acute- ness of muscle atrophy [78]. An example is Anderson and Bischof's system, who developed an AR system involving a virtual arm overlaid on a patient's residual limb and controlled by residual limb muscle activity [88]. This system, when compared to traditional, non-AR game-based systems, showed higher user experience and investment as well as comparable muscle isolation. Furthermore, the advantage of the virtual arm enables the patient to start the rehabilitation process earlier.

Another issue with current rehabilitation in upper limb amputees is the lack of a comprehensive objective assessment of the patient's progress. Commonly used methods to evaluate patient progress include the Box and Block Test (BBT) [89], the Southampton Hand Assessment Procedure (SHAP) [90], and the Clothespin Relocation Test (CRT) [91].

However, these are standardized tests only evaluating performance within a small range of movement tasks with limited degrees of freedom (DOF). Their assessment methods only account for completion rate (number of tasks successfully accomplished), lacking a more comprehensive quantitative and qualitative assessment of the patient's performance. Monitoring run-time dynamics to provide a more comprehensive assessment is important for practitioners to evaluate how well the patients are restoring mobility [92].

Hunt et al. developed the Prosthetic Hand Assessment Measure (PHAM), an alternative method to quantitatively assess performance in a range of manipulation tasks associated with object manipulation for upper limb amputees [93]. PHAM uses Inertial Measurement Units (IMUs) for motion tracking and presents a performance evaluation assessment metric that accounts for compensatory movements in the patient. Another method proposed by Yu et al. utilizes a Kinect-based system to introduce a personalized range of motion measurement with AR feedback [94]. The goals of the study were to establish the accuracy of the Kinect in measuring clinically relevant movements in patients with Parkinson's disease. The results of this system match experts' observations and show promising results for telerehabilitation scenarios [94], as well as, once again, the potential of rehabilitation within an AR system. As shown in the study by Yu et al., as well as later in Upbeat's [95] implementation, integration of motion tracking and electromyography (EMG) sensors within an AR system provides quantitative data physicians can use for objective assessment of patient progress. The flexibility of such a system also allows the therapy to be personalized to each patient's unique needs.

2.1.7 Amputee Rehabilitation - Phantom Limb Pain

Phantom limb pain (PLP) is commonly classified as neuropathic pain following amputation, brachial plexus avulsion injury, or spinal cord injury and is often resistant to pharmacotherapy and traditional rehabilitation techniques [96]. Previous systematic reviews have high- lighted the lack of evidence for pharmacological and non-pharmacological intervention in PLP treatment [97,98]. Patients suffering from PLP commonly experience a phantom limb that is paralyzed or fixed in one or more positions [99]. Recent quantitative studies revealed that PLP patients commonly exhibit impaired voluntary movement in their phantom hand [100,101]. Thus, neurorehabilitation techniques such as the Mirror Visual Feedback (MVF) method have been conducted in clinical practice to restore phantom limb movement [102,103].

Randomized controlled trials (RCTs) revealed the clinical importance of rehabilitation with MVF for alleviating PLP in lower and upper limb amputees [104,105]. Combining virtual reality (VR) technology with MVF treatment (VR-MVF rehabilitation) has been pro- posed to provide greater sensation of phantom limb movement and improve the alleviation of PLP [106–108]. These neurorehabilitation techniques have consistently suggested the importance of restoring voluntary movement of a phantom limb as the underlying mechanism of PLP alleviation [102,109,110]. However, the analgesic effects of VR rehabilitation have varied between previous studies [111,112].

The present results suggest that the variability in the VR rehabilitation effect re- ported in previous studies may have been related to differences in the causes of PLP and differences in PLP characteristics between subjects, reflecting the pathological mechanisms underlying PLP. Because PLP is thought to arise from multiple pathological mechanisms [96], previous researchers have emphasized the importance of mechanism-based management for the disorder [113]. Although VR rehabilitation for PLP has become relatively widespread [108,114], the rehabilitation technique does not appear to be effective for all patients, but most particularly VR-MVF treatment for improving PLP associated with distorted phantom limb movements and fixed posture [115].

2.1.8 Upper-limb Dysfunction

Upper-limb dysfunction is a common neuromotor impairment in patients with brain injury. Impaired muscle activation and motor control have a negative impact on motor training of the upper limb for functional skills, which are related to performance of activities of daily living. This may restrict social participation and diminish quality of life.

Traditional conventional occupational therapy is effective in improving upper-limb function but is resource-intensive. To achieve significant improvements, longer duration and high repetitions are required [116]; however, sustaining engagement with repetitive task practice can be challenging for patients, especially children. For this purpose, VR is being explored as an alternative treatment modality [117–119]. VR-based motor rehabilitation offers repetitive intensive tasks with immediate sensory-motor feedback on performance, which is an important learning component. Additionally, using virtual reality games aimed at stimulating motivation and attention within an enjoyable and playful environment, as well as adjusting task difficulty according to the user, may be an attractive option for children [117,120], allowing them to actively participate in rehabilitation.

Many studies have investigated VR/AR for motor rehabilitation post-stroke and in patients with Cerebral Palsy (CP). In a systematic review of research in rehabilitative VR for pediatric CP patients, a study found evidence of moderate efficacy for balance and overall motor improvements, but limited efficacy for specific motor skills [121]. However, they posit that the contextual diversity offered by virtual environments may support long-term engagement with regimens.

However, the role of virtual reality in improving hand function in children with cerebral palsy (CP) was unclear due to limited evidence; thus, virtual reality may be best used as an adjunct to other therapies [122]. Choi et al. conducted a randomized controlled trial, and the results of showed that virtual reality training was more effective than conventional occupational therapy in improving dexterity, performance of activities of daily living, and active forearm supination motion in children with chronic brain injury, especially those with severe motor impairments. A virtual reality rehabilitation system with wearable inertial measurement unit sensors was as effective as conventional occupational therapy for upper-limb training in children with brain injury including CP [123].

2.1.9 Perioperative Rehabilitation in Orthopedic Patients

As a population rapidly ages, the demand for orthopedic surgery also rises, especially joint replacement (e.g., total knee arthroplasty and total hip arthroplasty) [124]. Studies have shown that the elderly population undergoing orthopedic surgeries experiences higher percentages of complications and morbidity compared with their younger counterparts [125–127]. In addition to common complications pulmonary complications may occur [128]. Postoperative pulmonary complication (PPC) is defined as respiratory complications occurring within 48–72 hours after surgery [129], such as atelectasis, pneumonia, bronchitis, and bronchospasm [130]. Preoperative risks of PPC include older age (>65 years), smoking, chronic obstructive pulmonary disease (COPD), and bronchial asthma [129]. PPCs may increase morbidity and mortality, lengthen hospital stay, and further increase the health insurance burden [131].

Perioperative rehabilitation is crucial for patients receiving surgery to reduce complications and mortality [132]. Considering reducing PPCs, a guideline from the American College of Physicians suggests deep breathing exercises or incentive spirometry as postoperative interventions to be administered [133]. Preoperative rehabilitation including aerobic exercise, breathing exercise, and inspiratory muscle training has also been recommended [134]. The rehabilitation mentioned above could be delivered via health education leaflets, prerecorded videos, verbal instruction, one-to-one therapist supervision, or onsite training [135]. However, there are some disadvantages of these conventional programs, including a low retention of the educational content, lack of supervision or accuracy, inconvenience for rural residents, and lack of motivation [135]. Wang et al. conducted research within this domain and found that their AR app may add benefit to perioperative rehabilitation in orthopedic patients by enhancing pulmonary function [136].

2.1.10 Multiple Sclerosis

Multiple Sclerosis (MS) is a chronic, autoimmune disease of the central nervous system. MS commonly occurs in patients between the ages of 20 and 40, of which females suffer from two to three times more often than males [137]. MS is a global disease with its highest prevalence in Western Europe, North America, and Australasia, with an incidence greater than 100 per 100,000 inhabitants [138]. The most common subtype of MS is relapsing-remitting multiple sclerosis (RRMS), accounting for approximately 85% of all cases. The illness leads to progressive physical and mental disability. The most common deficits during MS include motor disability, visual impairment, cognitive decline, and sphincter disorders [137]. All these ailments lead to progressive limitations in everyday functioning, professional absenteeism, and social exclusion. Thus, even the slightest amelioration of the patient’s health or mitigation of the MS symptoms can bring a tremendous amount of comfort and relief.

Previous works often remark about the potential and advantages of immersive technology to provide tools, and environment for home-based rehabilitation [139–141]. The computer system can almost entirely supervise such a process, and an expert would periodically assess only the treatment results. Over the past two decades, there have been several studies concerning telerehabilitation facilitated with immersive interfaces.

For instance, an AR-based system for hand movement rehabilitation was proposed by Shen et al. [142,143]. Here, the authors used gloves for the acquisition of patient’s data, whereas the AR interface provided visual feedback and additional stimuli to the patients. A specially designed glove was also used by Lipovský et al. [144] for the self-hand rehabilitation process. Other authors [145,146] used Virtual Reality (VR) as a means of upper limb prosthetic rehabilitation. There are many more examples of immersive interfaces [140, 147,148] being used in the recovery of motor functions of the patient’s upper limbs, which typically involve some form of arm stretching and grabbing [140,144].

Pruszyńska et al. investigated the effectiveness of using a commercially available AR system in MS patients’ treatment and conducted a medical study with 30 MS patients undergoing immunomodulatory treatment. They reported that rehabilitation enhanced with AR significantly improves the strength and efficiency of the patients’ upper limbs. Furthermore, they inferred that AR-enhanced systems are a promising possibility of training without leaving home [149].

2.1.11 Psychological Therapy

In the field of psychology, both VR and AR have been combined with exposure therapy - recreating the fear/anxiety-inducing stimuli (Virtual Reality Exposure Therapy, VRET, and Augmented Reality Exposure Therapy, ARET); and cognitive therapy using a virtual coach voiced by a real therapist to augment the treatment of different kinds of phobias and anxiety, cravings for various substances (e.g., cigarettes, cocaine), post-traumatic stress disorder (PTSD), depressive symptoms, and distorted body image in case of anorexia nervosa. The effects are often transferred successfully in everyday life and maintained for months or years, maybe because AR and (mostly) VR allow the simulation of an ecological environment where every exposition cue can be entirely controlled [14,150–153].

For social phobia, VR is slightly inferior to in vivo exposure therapy, possibly due to the difficulties in recreating credible social interactions [151] or the uncanny valley hypothesis—briefly, feeling eeriness and aversion toward characters/avatars that closely resemble humans but show “non-human” features (e.g., moving robotically or having “cold” eyes) [154,155]. Moreover, VR is useful to reduce anxiety and pain during medical procedures (e.g., immunization, surgery, and oncological care), thus acting as a powerful distraction [156–159]—the greater the immersive experience, the greater the effects [160].

2.2 Factors of Consideration

In the literature, it has been found that the main uses of these technologies fall into two main areas: motor neurological rehabilitation [161–163] and training for prosthesis control [164,165]. It is also worth noting that VR and AR are used mostly as add-on therapies combined with already established treatments. Indeed, VR and AR seem to enhance the conventional therapies’ effects through the intensification of experience induced by gamification and realistic simulations [14,28,29,33,151]. Lastly, by recreating certain events (e.g., phobias and falls) in a simulated environment, VR and AR could also help understand the causes of psychological and neuromotor disorders and the stimuli that trigger them, allowing practitioners to deliver the therapy that best suits their patients [14,37,166].

VR/AR interfaces should also comply with certain conditions, i.e., no significant lag time to perceive it as a real time interaction, have seamless digitalization, use a behavioral interface (sensorial and motor skills), and have an effective immersion as close as possible to reality [167]. The use of virtual reality technologies for rehabilitation purposes has recently increased [161,168–170], especially for motor rehabilitation applications [171, 172].

There are also potential disparities between a system’s definition of difficulty and the participants’ perceptions of difficulty. For any individual participant, the system definition of difficulty could be more easier or difficult than the participant’s own experience when using the system [173]. Understanding and incorporating patient perceptions of difficulty in real-time is critical to successful rehabilitation intervention.

While visual realism may not be required for a system to be useful, visual fidelity may be. Allen et al. found that correct occlusion of virtual elements with real-world objects the users own hands, have an impact on user acceptance [174]. Advances in AR headsets, such as the infrared camera on the HoloLens, will allow applications to correctly mask virtual elements being handled by the user.

Conventional physical therapy (CPT) and VR/AR therapies are also believed to have a symbiotic relationship, where the latter increase patients' engagement and help them immerse in therapy, while CPT stimulates tactile and proprioceptive paths by means of mobilization, strengthening, and stretching. Therefore, the combination of both approaches could be beneficial to patients, bringing a more comprehensive and integrated treatment that can be clinically useful [175].

Virtual reality (VR) technologies have been explored as a possible adjunct to physical rehabilitation programs [176–184]. An example of such technology is the use of biofeedback in the form of VR games wherein patients, by participating in the game, improve motor performance. The advantages of this technology include graded levels of difficulty, ability to monitor task duration and intensity, provision of feedback on errors, and provision of tips and guidance on the movements performed [185].

It is important to remember that rehabilitation is a multi-disciplinary and multi-modal endeavor and not a 'one size fits all' intervention. A combination of interventions may be better suited to treat the multifactorial nature of the disability associated with neurological conditions, such as motor and sensory impairments, cognitive problems, and psychological issues. Veerbeek et al. recommend that robotic therapy is seen not as a 'standalone therapy' but is integrated into a comprehensive rehabilitation program [186].

2.3 Combination of Technologies

The combination of VR and robotic technology is particular interesting as it can theoretically activate more of the neural circuits involved in motor learning, and hence promoting neuroplasticity [187,188]. Several controlled trials have investigated the combination of VR and robotic technologies in upper-limb rehabilitation. Thielbar et al. investigated the use of a robot-assisted finger training system linked to the movements of a virtual hand and found a significant improvement in upper-limb activity and task performance compared to controls [189]. Byl et al. examined a robotic orthosis in a virtual training environment and found no between-group differences [190].

Unfortunately, not only did both studies have very few participants but both used a control group of physical therapy only, which makes it impossible to determine if any benefits identified are related to the combination technology or simply one of its components, e.g., the robotics. Klamroth-Marganska et al. looked at the effects of the exoskeleton robot ARMin, which provides intensive task-specific training in a virtual environment, as compared to conventional therapy, and found a small benefit in the Fugl – Meyer upper-extremity scale which was not clinically significant [191]. Whilst this trial had a moderate sample size, it again compared the combination technology to physical therapy only.

Early work by Mirelman et al. with participants with lower-limb impairments found that in individuals given combination VR and robotic therapy, compared to robot therapy alone, there was a significant increase in walking speed and distance [192]. Furthermore, individuals reported less fatigue in the sessions, required shorter rest time and fewer therapist cues, despite the number of repetitions being the same. Uçar et al. examined the effectiveness of the Lokomat device, a treadmill and lower-limb robotic exoskeleton combination together with a virtual reality screen display, as compared to conventional therapy [193]. They found a significant improvement in the Timed Up and Go test and the Ten Metre Walk test in the intervention group as compared to the control group.

2.4 Importance of Feedback in Rehabilitation

It is recognised that feedback plays an important role in skill acquisition and is an essential element in experience-dependent plasticity [194]. In motor learning, it is important to receive feedback not just on the end results – 'success or failure' – but on movement performance [195]; this is possible with the use of VR technologies. Feedback is very important during rehabilitation of new neuromotor pathways since it helps the user to correct the di- rection of the movement or intention towards the right track [161,164,196–199]. Instant feedback tells the brain and the body how to re-calibrate in the same way that it learned it the first time [196]. Moreover, as the user interaction in rehabilitation systems grows to- wards a closed loop approach, there is a need for a wider variety of feedback strategies, whether in the form of visual and audio-visual [200], tactile [201], or haptic [202].

Some studies have investigated technologies for in-home rehabilitation that center logistical barriers and confidence support in their designs. "Link Lights" was a portable light array that allowed patients to practice ocular motor and vestibular exercises anywhere in their homes with confidence, as the lights showed them where and when to look without ambiguity [203]. "Magic Mirror Spiral" allowed patients to see video of themselves correctly performing exercises in-clinic superimposed over themselves in-home [204]. This feedback assured them that they were doing their exercises correctly.

Informational feedback may be more important than reward systems in mediating patient adherence and competence. Yoo et al. found AR informational feedback significantly improved balance, gait features, and fall reduction for their intervention group, over the control group that did not receive visual feedback via AR [205]. Tretriluxana et al. investigated different feedback mechanics and noted that when patients can compare their motion path against an ideal path, motor function improved significantly over patients who could only see whether they had successfully completed the move or not [206]. These results demonstrate that technologies such as AR are a compelling context for informational feedback which can improve efficacy in executing regimented exercises.

Multi-modal feedback, such as the combination of visual, tactile, and audio feed- back [141], may support enhanced internalization of exercises as well as afford greater accessibility for users with sensory impairments. Embodied feedback, such as the combination of tactile feedback with visual information projected onto the body [141,207], may be more effective than the mirror approaches common in most work.

Furthermore, the control of the interface and the feedback received by the user are crucial to stimulate neurological pathways that aid in cases like neuromotor rehabilitation [208,209], for instance as in learning how to use a new prosthetic device [210].

2.4.1 Usage of sEMG as Feedback

The use of sEMG signals as a control strategy has been widely explored in the myo-electric prosthesis research area, but it is not until recent years that these control techniques have migrated towards other therapy applications, for example, in the control of computer interfaces and environments such as VR and AR [211]. sEMG signals bring about the possibility of a complex multichannel/multiclass type of control algorithm that enables, in turn, the implementation of more intuitive user interfaces for the patient to perform [212]. This is important as it closes the loop of control/feedback interaction, and this special quality promotes neuroplasticity pathways to emerge [213]. However, the use of biosignals in VR/AR applications requires more effort than other control strategies that involve other sensor measurements or motion analysis.

On one hand, sEMG signals have been widely explored for control purposes [214] and, on the other hand, VR/AR interfaces have been explored to improve the outcomes of physical rehabilitation therapies [81,215]. Furthermore, as mentioned above, several feedback techniques have been considered recently, but mainly as sensors that record a variable and return a quantitative measure to the experimenter or provide the user feedback that might feel unnatural [200–202].

Literature suggests that using sEMG signals to control VR/AR interfaces can pro- vide better outcomes when paired to CPT. In 2018, Meng et al. [216] performed a 20-day follow- up experiment to prove the effectiveness of a rehabilitation training system based on sEMG feedback and virtual reality that showed that this system has a positive effect on recovery and evaluation of upper limb motor function of stroke patients. Then, in 2019, Dash et al. [217] carried out an experiment with healthy subjects and post-stroke patients to increase their grip strength. Both groups showed an improvement in task-related performance score, physiological measures (using sEMG features), and readings from a dynamometer; from the latter, both groups gained at least twice their grip ability. Later, in 2021, Hashim et al. [218] found a significant correlation of training time and the Block Test score when testing healthy subjects and amputee patients in 10 sessions during a 4-week period using a videogame-based rehabilitation protocol. They demonstrated improved muscle strength, coordination, and control in both groups. Moreover, these features added to induced neuroplasticity and enabled a better score in this test, which is related to readiness to use a myoelectric prosthesis. More recently, in 2022, Seo et al. [219] proposed to determine feasibility of training sEMG signals to control games with the goal of improving muscle control. They found improvement in the completion times of the daily life activities proposed; however, interestingly, they report no significant changes in the Box and Block Test.

Literature supports the hypothesis that sEMG signals can be a robust biofeedback method for VR/AR interfaces that can potentially boost therapy effects. On top of an in- creased motivation and adherence from patient to complete rehabilitation therapies [218], the method also yields a different type of awareness to the patient of their own rehabilitation progress. Furthermore, this type of therapy offers quantitative data to the therapist, potentially allowing a better understanding of patient progress, which brings certainty to the process.

Nonetheless, sEMG signals as control or feedback of a VR/AR interface merge has not been investigated thoroughly, and even less so in the form of a systematic literature review (SLR). sEMG signals can be better interpreted by patients as control and the visual feedback completes the natural pathway they lost and are trying to get back through rehabilitation therapy. There are some SLRs that have analyzed VR and AR interfaces used for hand rehabilitation, but some lack an adequate inclusion of feedback techniques [20], whereas others include feedback and focus on the similarity of techniques among VR inter- faces for rehabilitation therapy and CPT [175]. Some studies use a computer screen interface to address virtual rehabilitation therapies [220].

Although some studies show sEMG signals paired with VR/AR environments, just a few discuss if there are advantages in clinical results compared to conventional therapy groups, and there is a shortage of standardized protocols when sEMG signals are used for rehabilitation therapy purposes [211,221,222]. Hence, there is not enough information in the literature to determine if these biosignals used as control or feedback of VR/AR systems improve the positive outcomes of neuromotor rehabilitation therapies and whether they promote, e.g., neuroplasticity or support training of myoelectric control for prosthesis fitting. It is also important to know if the hardware used is commercially available or proprietary/developed, and if the signal processing techniques used are similar enough to be compared. Likewise, it is important to learn the rehabilitation target to which this technology has been applied to and if they have been tested with healthy subjects or patients, and if this technology is aimed for a clinical environment or only for research protocols. [223] gave a SLR which provides a global framework of the most common application of sEMG signals for control/feedback of VR/AR interfaces and found that the use of these signals for rehabilitation is still scattered and heterogenous.

3 Methods

3.1 Virtual Reality Systems Overview

Immersion in VR is the effect caused by a situation, environment, or graphic representation which makes the user perceive the projected environment as reality. Jennett et al. [224] define VR in terms of user involvement; and consider it as the reason behind lack of awareness of time and actual world, along with a feeling of “being” in the work surroundings. While talking about immersion in general VR cases, the term “spatial immersion” is used, which means being physically present in a fabricated environment. This occurs when a user’s senses are partially/ fully stimulated by a VR system using images, sound, and other feedback sources to feel the said world as real. Considering an important element of a VR system, the levels of immersion can be varied for different purposes. The three primary categories of VR simulations, differentiated on the degree of immersion, are outlined further.

3.1.1 Non-Immersive VR

Non-Immersive VR allows the subject to interact in a simulated world and can be straight-forwardly deployed using input devices like joystick, monitor, keyboard, or a mouse [225]. Even though it is a computer simulated world, the user is well-aware about the surroundings and can control aspects of this environment. Non-immersive systems are also considered economic and are generally easier to set up as compared to immersive VR. Video game systems or movie systems are common examples of this system. Non-immersive VR is also used in rehabilitation, for instance, a RAPAEL smart glove experience developed by Lee et al. [226] proved beneficial to improve the upper limb function of stroke patients.

To reduce fall risk and improve gait rehabilitation in older adults, a non-immersive VR system with a motion-capture (MOCAP) camera setup and a computer-aided simulation demonstrated positive results [227]. The VR system consisted of a motion-capture camera and a computer-generated simulation projected on to a large screen, which was specifically designed to reduce fall risk in older adults by including real-life challenges such as obstacles, multiple pathways, and distracters that required continual adjustment of steps. Non-immersive VR systems are therefore considered as a powerful tool to improve neurological disorder-related symptoms and to elevate cerebral and motor function of the brain.

3.1.2 Semi Immersive VR

Semi-immersive simulated practices provide the feeling of presence in a different certainty while still staying aware of the surroundings. Quality details of the graphic along with the feedback provided by the system are directly proportional to the immersive feeling. Hardware for these systems generally includes high-resolution screens, powerful processors, and projectors to partly imitate the design and functionality of practical real-world scenarios. This class of VR is often utilized for educational or vocational training. Studies suggest that semi-immersive VR could be a beneficial approach for therapy of patients with traumatic brain injury, potentially leading to better cognitive and behavioral outcomes [228].

3.1.3 Fully Immersive VR

Fully immersive is the most realistic simulation experience to perceive and indulge with complete immersion-based virtual reality, where the operator needs the relevant supporting tools. VR headsets are most used to offer high-resolution data with a varied field of view for a surreal immersive VR experience. The display creates a stereoscopic 3D effect and follows with the input tracing and feedback to create an authentic experience. A Cave Automatic Virtual Environment (CAVE) is a completely immersive VE wherein the user wears 3D glasses and is surrounded by projection screens or flat displays. It is also widely used for education and training purposes [229]. VR glasses and Head Mounted Dis- plays (HMD) deliver visual and auditory cues in the form of detailed graphics and auditory information. In addition to the benefits mentioned above, VR systems like Oculus Rift also allow for precise tracking of the user's movements, thus making it very useful for education, training, and rehabilitation purposes [230]. While CAVE systems are more expensive and difficult to move, HMD, VR glasses, and Oculus Rift are relatively cheaper and easy to handle.

3.2 Augmented Reality Systems Overview

AR can be explained as a modification of the actual environment by adding visual or sound or other stimuli to it. The user interacts with the digital world and the system makes the changes to the world by augmenting elements to it. Edwards-Stewart et al. [231] classify AR systems into two main categories-triggered and view-based augmentation. Triggers refer to characteristics like object markers, GPS location, and dynamic augmentations of objects that initiate the augmentation.

3.2.1 Trigger-Based Augmentation

Trigger-based AR comprises Marker-based AR, Location-based AR, Dynamic Augmentation, and View-based AR. Marker-based AR can be either object based, or paper/ image based. The object or image containing the marker is called the trigger object and it can be recognized by the AR system upon scanning. The scan triggers an additional sequence where more relevant content can be displayed on the device. Marker-based AR has been instituted successfully with patients suffering from animal phobias. Location-based AR is geo based and marker-less — it relies on GPS, accelerometer, digital compass, and other technologies to accurately identify a device's location. Dynamic AR, usually included with motion tracking, is receptive to the object's view as it alters. Lastly, the fourth kind of triggered AR is complex augmentation, defined as a hybrid form of location-based AR and dynamic amplification. A popular example of this is Google Glass, where users can access information regarding local spots depending upon their GPS location [231].

3.2.2 View-Based Augmentation

View-based AR consists of Indirect AR and Non-specific Digital AR. Indirect AR means augmenting static images as per the user's preference. For example, trying on clothes virtually by superimposing clothes onto an existing image of the person. Non-Specific Digital AR refers to digitize a dynamic outlook of the environment without having any reference to what is being perceived [231]. This is a common policy to be found in mobile games. The operator intermingles with the augmentation like tapping the augmented scenarios upon viewing without having a reference to the operator's surroundings. However, it is pertinent to mention that view-based augmentation is not considered to be a part of AR in accordance with Milgram et al. [232].

3.3 Virtual and Augmented Reality Systems in Medical Rehabilitation

Shin et al. [233] conducted a single-blinded randomized controlled trial aimed to examine the effects of VR-based rehabilitation combined with standard occupational therapy on distal upper extremity function and HRQoL. They used RAPAEL Smart Glove^{TM} (Neofect, Yong-in, Korea), as shown in Figure2, which is a biofeedback system designed for distal upper extremity rehabilitation in stroke survivors. The sensor device tracks the motion and posture of the wearer's distal limb and recognizes functional movements, such as forearm pronation/supination, wrist flexion/extension, radial-ulnar deviation, and fin- ger flexion/extension. An inertial measurement unit sensor in the device measures the 3-dimensional orientation of the distal limb, and 5 bending sensors estimate the degree of bending of the fingers. The gathered sensing data is transmitted and received via wireless communication systems such as Bluetooth. The software application manipulates virtual hands or virtual objects in training games according to the received data. In addition, this system can evaluate the active and passive range of motion for each functional movement.

The difficulty of the intervention was adjusted by occupational therapists according to participant performance. They held a total of 20 sessions over a 12-week period and found significant score improvements in the treatment group than in the conventional therapy group. The study noted greater improvements in multiple outcomes of the distal up- per extremity, including motor impairment (FM-total, FM-prox, and FM-dist scores), hand functions (JTT-total and JTT-gross scores), and HRQoL (composite SIS, overall SIS, SIS- social participation, and SIS-mobility scores) using VR-based rehabilitation with standard OT than using amount-matched conventional rehabilitation, without any adverse events, in stroke survivors.

Waliño-Paniagua et al. [234] conducted a single-blinded randomized controlled trial aimed to analyze an occupational therapy (OT) intervention compared with OT + VR on the manual dexterity of patients with MS. They used the online web page motiongamingconsole along with a video camera to administer the VR treatment, which involved games such as Flip Out, Air Hockey, Particles, DunkIt, Counting Fish, and Robo Maro. The patients attended 20 sessions with a frequency of 2 per week, where 30 min of OT and 20 minutes of VR gaming via the website was provided. Clinical improvements were found regarding the precision of movements, the execution times, and the efficiency of certain functional tasks in the OT + VR group.

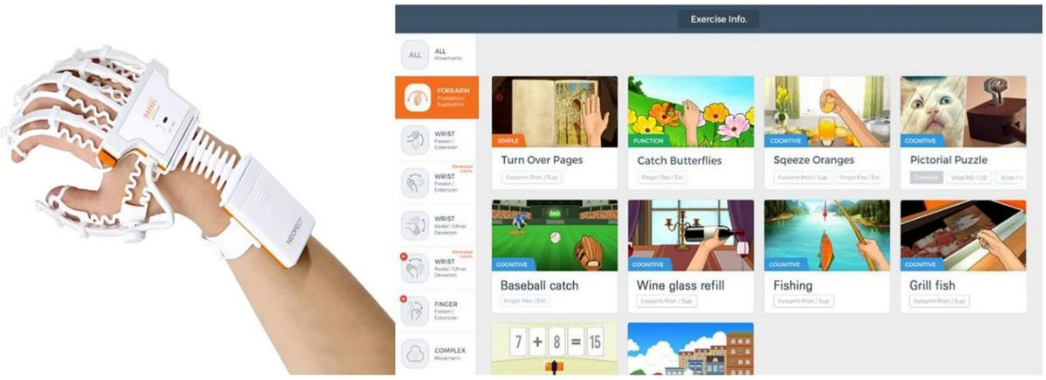


Figure 2: Task-specific games of system [233] including catching butterflies or balls, squeezing oranges, fishing, cooking, cleaning the floor, pouring wine, painting fences, and turning over pages.

Wu et al. [235] conducted an intervention study to examine if Leap Motion Control (LMC), a kind of virtual reality games which employs a novel system that provides biofeedback and training of fine motor function and functional skills, would improve burned hand function. They used LMC and a laptop to administer LMC games such as cube grasping, flower petal removal, and balloon or bird shooting. This was administered for 2 days per week over a period of 4 months, where 40 min of occupational therapy (OT) plus 20 min of VR in LMC group was provided. Results showed improvements in treatment group over control group, with increased ROM of thumb IP joint and pinch strength and decrease in scar thickness over the first dorsal interossei muscle in LMC group.

Standen et al. [236] conducted a randomized controlled trial to assess the feasibility of a home-based virtual reality system for rehabilitation of the arm following stroke. The intervention was a virtual glove consisting of a hand-mounted power unit, with four infrared light emitting diodes mounted on the user's fingertips. The diodes were tracked using one or two Nintendo Wiimotes mounted by the monitor on which the games were displayed to translate the location of the user's hand, fingers, and thumb in three-dimensional space. The participants played Spacerace (guide a space craft through obstacles), Spongeball (release a ball to hit a target), and Balloonpop (pop balloon by moving it to a pin protruding from the virtual floor), where users had to perform the movements of reach to grasp, grasp and re- lease, pronation and supination that are necessary fort many activities of daily living. This intervention was administered for 3 days per week for a period of 8 weeks, and patients had the virtual glove in their homes and were advised to use the system for a maximum of 20 minutes. The study reported significantly greater change from baseline in the intervention group.

NeuroR [73] is a post-stroke rehabilitation system based on AR technology. The system provides motor imagery, which can be defined as "the mental execution of a movement without any overt movement or without any peripheral activation, by means of a virtual 3D arm that replaces the paralyzed arm in a virtual avatar of the patient. It can be used either in rehabilitation centers as well as at home. The system setup is shown in Figure 3, which includes exercises to achieve ROM of flexion and abduction of the shoulder. The AR Rehab Systems uses marker-based AR technology that uses the recognition of a distinguishable element, which can be identified apart from other objects in the environment by means of a camera. The virtual object is displayed only if the corresponding marker is visible. Al- though this technology uses visually obtrusive markers, it can offer a better tracking (more precise and faster), thus it is used in numerous AR applications.

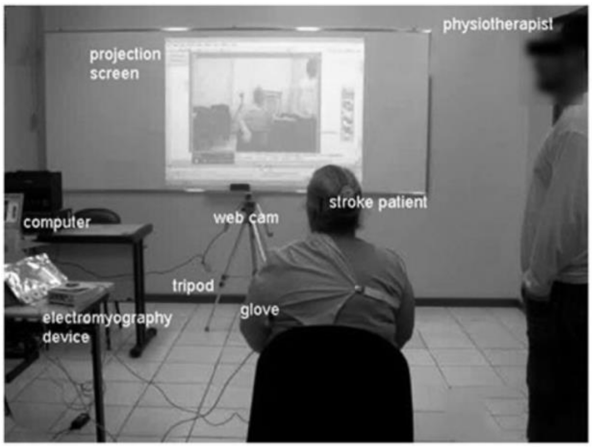


Figure 3: NeuroR System Setting for Shoulder Rehabilitation [73]

The markers employed were black-and-white (B/W) fiducial markers in the form of a pattern. It provided visual feedback to the patients using a projector, and audio feed- back using PC audio speakers. The authors of NeuroR conducted two studies. In the first study, they evaluated the effectiveness of the system on upper limb motor function using the Fugl-Meyer scale. The results of the Fugl-Meyer test suggested a trend for greater upper limb motor improvement in the augmented reality group (from 17% to 62%) than in the control group (from 4% to 14%). In the second study, they measured the increase of shoulder ROM with computerized photogrammetry. All participants showed an increase of the ROM for shoulder flexion (61.3% to 90%) and abduction (46.7% to 73.9%). However, a further large, randomized study is needed to support observed improvements.

SleeveAR [141,237] is a system that integrates multimodal feedback (visual-audio- haptic) to guide the patient through therapeutic rehabilitation exercises (abduction-adduction, elevation-depression, flexion-extension) prescribed by a physical therapist. The system pro- vides the patient a guidance for movements together with a report on the exercise progress by means of AR projections on their arm and on the floor, as shown in Figure 4. Specifically, motion capture technology, such as Optitrack [238] is used to track peoples' arm movement.

AR Sleeve system is designed for home settings; however, because of its complexity and high cost, at this time it can be used in rehabilitation gyms with multiple and concurrent therapeutic sessions.

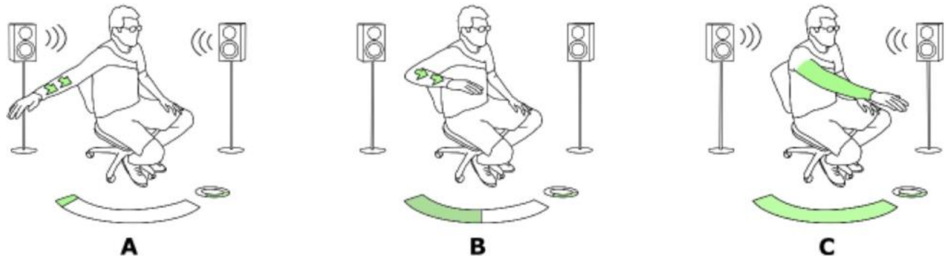


Figure 4: Patient following feedback given to execute a simple movement: A) The initial phase, combining audio and visual cues. B) Floor projected visuals follow the patient's movement in real-time. C) A completed exercise also triggers audio feedback. [141]

SleeveAR incorporates audio-visual-haptic trimodal feedback that is applied to guide and motivate the user during a task. Tactile feedback is used to notify patients of specific events (e.g., current state of the exercise). The AR interface in this system is a wearable device (MYO bracelet, North Inc., Canada) able to provide multiple ranges of vibrations in an easy and simple way via wireless communication. This provides real time feedback to guide the patient during the rehabilitation exercise and to maintain a quality in the execution of the task.

The authors of SleeveAR conducted a usability study to evaluate user performance: The results showed that the system can successfully guide subjects through an exercise prescribed (and demonstrated) by a physical therapist, with performance improvements between consecutive executions. The study included a comparison of two different approaches: AR system and video observation. Each test session involved the execution of five different exercises in the two approaches as the guidance: The video and with the SleeveAR. At the end of test sessions, all participants filled a six-point Likert questionnaire; results showed a statistically significant difference for the item "It was easy to see if the arm was in the wrong position", whereby it is noteworthy that participants gave higher assessment to the AR system.

AR Fruit Ninja [239] is an AR version of the popular "Fruit Ninja" game for patients with chronic stroke. The system provided participants with bimodal feedback (visual- audio) by using a projection-based AR technology and provided a game score. Figure 5 shows the experimental setup where the authors compared the user motor performances obtained with their system to those obtained using the original videogame "Fruit Ninja" without AR. Both required that the subject move the stroke-affected hand across the table- top to control the movement of a cursor that earned points by slicing fruit targets. Both versions of the game leveraged the same camera; however, in the PC version, game activity was displayed using a computer monitor, while in the AR version, game activity was displayed on the tabletop using a projector.

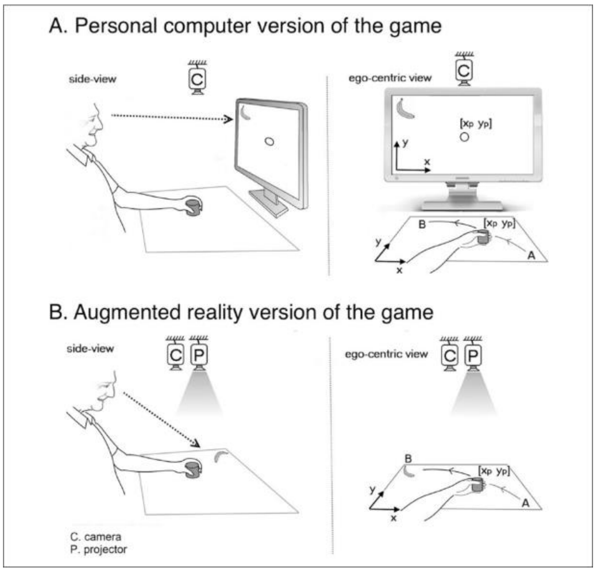


Figure 5: A patient playing the (A) personal computer (PC) and (B) the augmented reality (AR) versions of the Fruit Ninja game. Game features and movement demands were identical across the 2 versions of the game [239]

This difference imposed 2 key differences. First, during PC play but not AR play, the subject needed to perform an extra spatial transform to convert the coordinates of tabletop arm movements to the coordinates of the cursor movements seen on the monitor. Second, during PC play, eye and hand movements were uncoupled, with subjects receiving proprioceptive feedback but no visual feedback (gaze was directed at the monitor not their hand), while during AR play, visual and proprioceptive feedback were coupled. These differences likely account for the significantly poorer motor performances seen with PC play, as compared to the AR game where the scores were higher (21%), reaching times were faster (19%) and less movement variability was observed (15%).

MirrARbilitation [240,241] is an AR rehabilitation system, designed for patients after stroke and mastectomy, with gesture recognition based on marker-less body tracking technology, such as the Microsoft® Kinect™ motion sensing input device. The system uses a projector to provide visual feedback as a motivational tool to provide a funnier experience for patients, and guides and motivates the user during the execution of a reaching task, allowing the physiotherapist to set the target object angle. In addition, it provides score points and gives instructions to avoid the incorrect execution of movements. This system is specifically designed to fit within a home environment.

The real-time visual feedback integrated in MirrARbilitation is used to guide and correct patient movements during rehab sessions, to evaluate user performance, and for motivational purposes. Exercise instructions, as well as scores and positive feedback, are displayed on a standard screen during therapy sessions. In addition, once more for motivational purposes, X-ray images of the shoulder anatomy are superimposed during the interval of motion. The real-world image is obtained directly from the Kinect's RGB camera. The movement begins with the user catching the object during a resting position (taking the ball) and ends when it is placed at the target position (basket), as shown in Figure 6. These objects were used to trigger and induce the movement and also to add a lucid aspect making our system more attractive.

Figure 6: MirrARbilitation elements and interface (A to C); Reaching and catching game dynamics (D, E); End of level with congratulations message (F); Warning and instruction for wrong movement's performance (G to I) [240]

MirrARbilation was evaluated on objective (performance analysis) and subjective measures (via questionnaire) on 33 participants in the study. The authors showed that their application is more efficient than traditional rehabilitation methods because it improves the user engagement and the exercise performance outcomes. The motivational and usability aspects were evaluated by means of a five-point Likert questionnaire. In addition, the increased motivation of the users was shown by the number of exercise repetitions that was improved from 34.06% to 66.09%. On the other hand, the exercise performance outcomes were showed from an increase percentage of correct exercises from 69.02% to 93.73%.

Colomer et al. [242] introduced an AR System that is a portable and low-cost mixed reality tabletop system for upper limb rehabilitation which is based on marker-less tracking technology using the Microsoft® Kinect™. This system allows multi-touch interaction with the hands or via manipulation of tangible objects, depending on the exercise selected. The exercises cover a wide range of hand and arm movements and involve ADLs (e.g., sweeping the crumbs from the table). In addition, the system provides bimodal feedback (audio-visual) of the user performance. The study evaluated the clinical effectiveness and the acceptance of an experimental intervention with the system in chronic stroke survivors by comparing it to conventional therapy.

Figure 7 displays the variety of exercises included in the AR System by Colomer et al. [242]. The exercises covered a wide range of hand and arm movements, mostly focusing on the flexion and extension of the elbow and the wrist. The study reported positive effects of the experimental intervention in both activity and participation, and also influenced the progression of the participants. The significant improvement in timed tests related to activity after the experimental intervention was highlighted, since task performance is considered an indicative of functional improvement in individuals with chronic stroke, and since movement speed and quality of movement are interrelated [242].

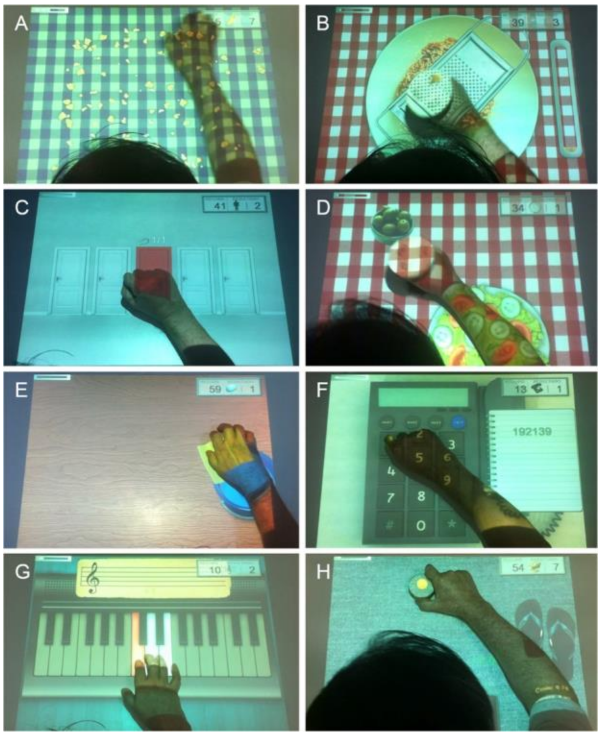


Figure 7: Description of the exercises in AR System [242]. a: to sweep the crumbs from the table, b: to grate, c: to knock on doors, d: to cook, e: to squeeze a sponge, f: to dial a number, g: to play piano, h: to buy items.

Norouzi-Gheidari et al. [243] conducted a pilot randomized clinical trial to examine the safety and feasibility of providing additional therapy using a VR exergame system and assess its preliminary clinical efficacy to improve motor function in stroke survivors. Figure 8 illustrates Jintronix, the virtual reality exergame system used in the trial to improve motor function in stroke survivors. All participants in the intervention group attended exergaming sessions at least twice a week for 4 weeks, in addition to the rehabilitation services they were receiving. During that time, participants spent on average an additional 21 min of upper limb exercising in each 45 min session of exergaming with minimal therapist supervision.

Figure 8: The Jintronix rehabilitation exergaming system [243]

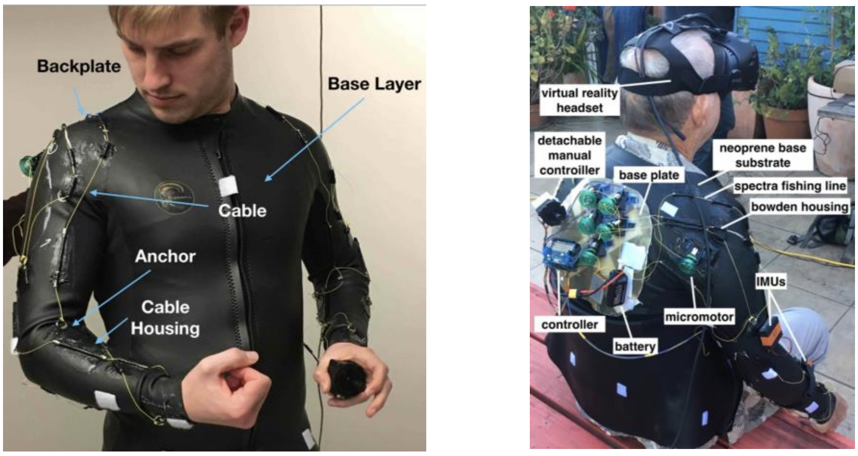
This system is an interactive exergame based on the Microsoft® Kinect™ camera, a marker-less motion tracking system. It differs from systems, such as the Nintendo Wii, which requires a wireless controller to detect the person's movement. Without wearing, holding, or using any sensor, the rehabilitation exergaming system uses the Kinect camera to track the upper and lower body movements in real time; this includes the person's head, trunk, arm, shoulder, elbow, wrist, and lower body movements on both sides when sitting or standing. The tracked motions are displayed in the gaming environment tailored for therapy. The system provides repeated unilateral and bilateral upper extremity training in all planes, at customizable difficulty levels: Speed, target size, precision, and predictability are all elements that can be programmed by the therapist based on the patient's abilities.

Conducting VRT in addition to CT, post-intervention improvements were observed in ADL measures. The efficacy measures showed statistically meaningful improvements in the activities of daily living measures (i.e., MAL-QOM (motor activity log-quality of movement) and both mobility and physical domains of the SIS (stroke impact scale) with mean difference of 1.0%, 5.5%, and 6.7% between the intervention and control group, respectively) at post-intervention.

Another VR visual feedback therapy via HTC Vive Head-Mounted Display (HMD) was explored in the study butterfly project by Elor et al. [244], which aimed to evaluate the feasibility, ease-of-use, and comfort of their proposed system. The users experienced physiotherapy by following and guarding a virtual butterfly, with the help of a robot-based wearable device to assist the subject's upper extremity movements. The designed exosuit, shown in Figure 9a, can lift the user's arm in different directions to create smooth multi-jointed movements. The concept of tensegrity for soft robotics inspired the mechanics of CRUX. Tensegrity (a portmanteau of "tensile" and "integrity") defines structures as internally prestressed, free-standing, pin-jointed networks in which the cables or tendons are held in tension against a system of bars or struts.

The suit's controller was designed to have the weak arm follow the movement of the healthy limb. This mirroring of limbs instigates mimetic controller design. Mirroring the movement from one side to the other side of the body was inferred from MVFT to increase motor recovery and stimulate brain plasticity. Figure 9b depicts the CRUX being fitted to a user by an evaluator for upper arm force amplification. To enable the mimetic control of the healthy arm onto the weak limb, wireless connectivity capability was added to connect with the Inertial Measurement Unit (IMU) networks. An IMU is an electronic device that measures and reports a body's specific force and angular rate using a combination of accelerometers, magnetometers, and gyroscopes. The IMU network added to the exosuit consists of 4 IMU nodes where each node can measure 3-axis orientation of itself and then send this data back to the microcontroller. The IMU nodes on CRUX are enclosed in a 3D printed case with adjustable Velcro straps to accommodate various body sizes.

Paired with an HTC Vive controller, the exosuit assists the user during VR game- play. Testing of the system targeted two pairs of motion primitives: elbow extension/flexion, and shoulder abduction/adduction. Biceps received assistance by replacing the user's CRUX supported HTC Vive controller as a bubble shield and having them protect the butterfly from incoming rain and projectiles through a therapist-specified customized range of motion path. Haptic feedback is enabled so that the user is indicated with strong pulses whenever the motion primitive was not followed (failure to encapsulate the butterfly inside the bubble). To increase the incentive and track compliance, the user receives a scoring point per every half second that they mirrored the required motion primitive. This multi-sensory feedback guided users according to the objective of the game.



(a) Demonstrator wearing CRUX (without IMUs). CRUX is an augmentative wearable soft robot for upper-extremity rehabilitation and can be combined with VR through Project Butterfly to enable immersive rehabilitation.

(b) A participant exploring CRUX. Control is achieved by using IMU Nodes and an internal controller for leader-follower mimicry. A user can control their impaired arm using their healthy arm to match the movement path.

Figure 9: Project Butterfly [244] equipment demonstrations.

Sánchez-Herrera-Baeza et al. [245] conducted a mixed methods intervention study for PD patients to evaluate the effects of a novel immersive virtual reality technology used for serious games (Oculus Rift 2 plus leap motion controller—OR2-LMC) for upper limb outcomes. Patients used LMC systems mounted on an OR2 device with their elbows positioned at an initial flexion of 90◦while seated at a table at mid-trunk height. The video games developed for this study were designed to empower depth perception to maximize the functional gains from the therapy. Individual sessions lasted for 30 min and were conducted three times per week over six weeks, for a total of 18 sessions per patient.

Patients performed the four video games in the following order (Figure 10): the reach game (RG), the sequence game (SG), the grab game (GG), and then the flip game (FG). The duration of each game depended upon the individual skill level of the patient, with the average duration of each game lasting approximately five to seven minutes. They observed significant improvements in strength, fine and gross coordination dexterity, and mobility speed in the impaired side with outstanding agreement.

Cuesta-Gómez et al. [246] conducted a randomised controlled trial to evaluate the effectiveness of the specially developed Serious Games that make use of LMC for improving upper limb (UL) grip muscle strength, dexterity, fatigue, quality of life, satisfaction and compliance in patients with MS. For this study, six serious games were developed by the UC3M authors, according to the guidelines provided by clinicians. The Leap Motion sensor was employed to capture the user's hand movements, and different virtual environments were created. Figure 11 presents some of the video games used.

Figure 10: The designed video games: the reach game, the sequence game, the grab game, and the flip game). Note: “Alcance” = Reach; “Agarre” = Grip; “Secuencia” = Sequence; “Cubos” = Cubes; “Volteo” = Flip. [245]

The experimental group received two 60 min sessions per week over a ten-week period plus 15 min of LMC with each session in addition to conventional rehabilitation. Grip muscle strength, coordination, speed of movements, fine and gross UL dexterity, fatigue, quality of life, satisfaction and compliance were assessed in both groups pre-treatment, post-treatment and in a follow-up period of 1 month without receiving any treatment. In the experimental group compared to the control group, significant improvements were observed in the post-treatment assessment for coordination, speed of movements, fine and gross UL dexterity. Also, significant results were found in the follow-up in coordination, speed of movements, fine and gross for the more affected side. Results also showed high satisfaction and excellent compliance.

Van der Meulen et al. [247] report on the design and evaluation of a serious game that engages patients with PD in upper extremity (hand/arm) movements. They developed a simple concept game that could be implemented using the Optical-See Through Head Mounted Display (OST-HMD). The game is situated in a candy factory where conveyor belts move the candies to be collected in a basket. The objective of the game is to catch the candies before they reach the front edge of the conveyor belt and fall into a digital void. The haptic game controller consists of a 3D printed handle with a cube that featured five tracking images (one on each side, except the bottom side), as shown in Figure 12.

Taesung In et al. [248] conducted randomized controlled trials to investigate whether Virtual Reality Reflection Therapy (VRRT) could improve the postural balance and gait ability of patients with chronic stroke. VRRT is an exercise that can be safely applied to people with stroke. Participants sit on a mat without back support, with both feet on the floor. Participants placed their affected lower limb into the VRRT box to observe the projected movement of the unaffected lower limb without visual asymmetry causing tilting of the head and trunk, as shown in Figure 13. The unaffected lower limb of each participant was placed so that the center of the camera was over the limb. Participants then adjusted the lower extremities so that the image was projected in the location of the affected lower extremities. When the program started, the participants were asked to watch the movements of the lower limbs on the monitor only.

They were then asked to move their unaffected lower limb at a comfortable speed. During the 4-week test period, three sets of 10 repetitions per motion were conducted for 30 minutes a day, five days a week in addition to conventional rehabilitation program. The first week was spent adapting to the VRRT, and every week thereafter, the level of tasks was consistently elevated to encourage the participants to take more interest in them. Either the caregiver or the participants, under observation of the guardian, could intervene in the program, and a checklist on the back of the equipment was used to ensure each step was completed.

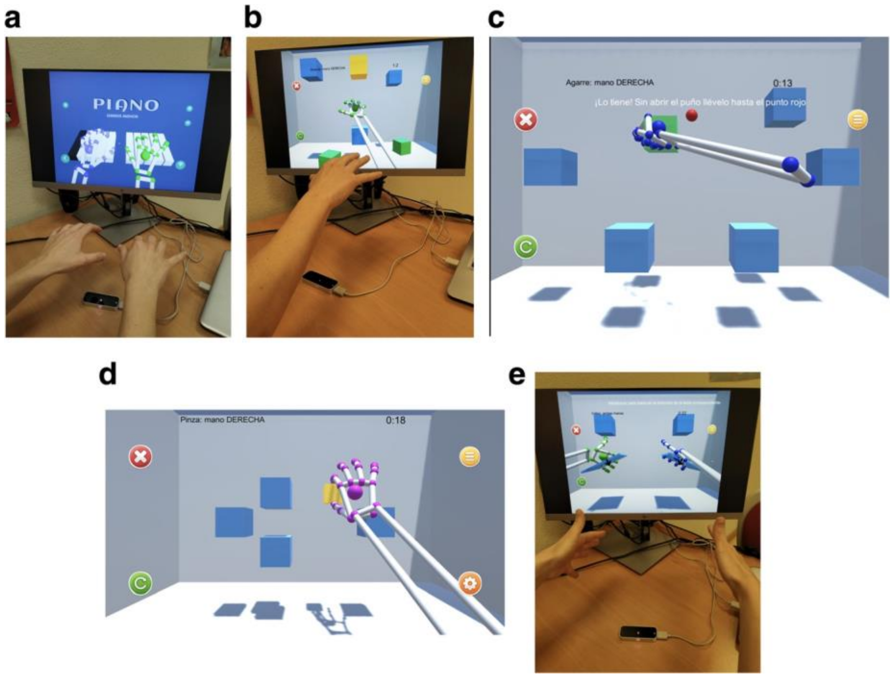


Figure 11: a Piano Game using both hands. **b** Reach Game using right hand. **c** Grab Game using right hand. **d** Pinch Game using right hand. **e** Flip Game using both hands. [246]

Figure 12: (Right) the OST-HMD and (Left) the controller used to play the game. [247]

Janeh et al. [249] conducted a pilot study to find a "virtual reality based" gait manipulation strategy to improve gait symmetry by equalizing step length for patients of PD. The gait parameters were measured using a GAITRite® electronic walkway system. A virtual mat in the virtual environment was placed that exactly matched the real GAITRite® system walkway. The virtual item correlates to the start (green line) and target (red line) lines were placed on the floor in front of the participant to indicate the walking distance in the virtual world as well as the real world. The system setup is shown in Figure 14.

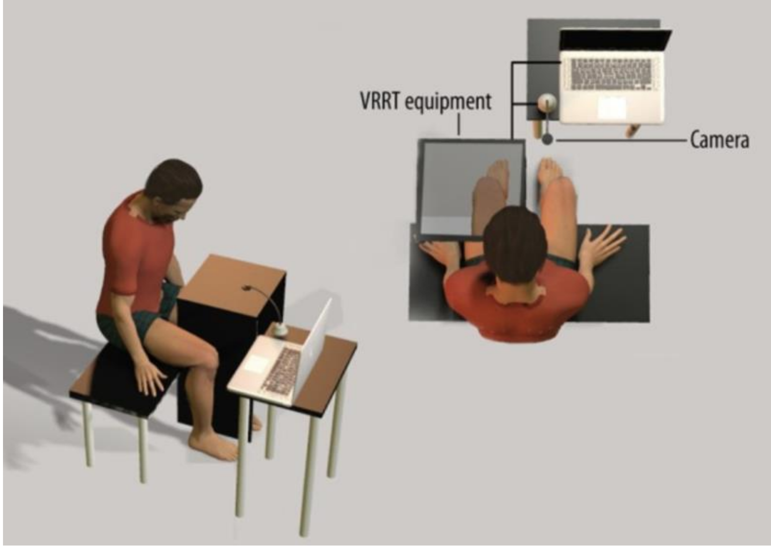


Figure 13: Setting for virtual reality reflection therapy. [248]

Participants were asked to first assume the start position by standing in an ortho- static pose at the start line. Then, participants were instructed to walk at their self-selected pace along the walkway of the GAITRite® system while stopping at the location of the target line (see Figure14b). After each trial, the participant had to walk back to the starting point alongside the GAITRite® walkway. During the experiment, an assistant managed the cables for each participant to provide comfort to the head from the weight of the cables. The main purpose is to find a method for equalizing step length asymmetry in PD patients. They found a significant step length difference between both legs in PD with FOG. The virtual dissociation of visual and proprioceptive signals was most promising in accomplishing this goal and might therefore be a sufficient rehabilitative technique to achieve gait symmetry.

Figure 14: Experimental setup: (a) A participant walks in the real workspace with a head-mounted display (HMD) over the GAITRite® walking surface. (b) Participant's view of the virtual environment on the HMD. [249]

Bergmann et al. [250] conducted a pilot randomized controlled trial to evaluate the acceptability of robot-assisted gait training (RAGT) with and without VR in non- ambulatory patients with a subacute stroke. The robotic-driven gait orthosis Lokomat (Ho- coma AG, Volketswil, Switzerland) was used for RAGT in both groups. The Lokomat is an exoskeleton with linear drives on hip and knee joints that assists locomotion on a tread- mill by guiding the subjects' legs along a predefined trajectory. Patients were fixed into the gait orthosis with a harness, which was attached to a body-weight support system, and had cuffs placed around the legs. Elastic straps were used to passively lift the subjects' feet and prevent any foot drops. tension on the straps was steadily decreased as motor recovery improved. body weight support was individually set for each patient, with no more than 50% of the patient's body weight.

Patients were randomly allotted for control groups (with standard RAGT) and intervention group (with VR augmented RAGT). Both groups performed 12 sessions (4 weeks, 3 sessions per week), and during the four-week intervention phase the amount of additional physiotherapy in the rehabilitation setting was controlled: all patients received 60 minutes of physiotherapy on the two working days without study intervention and no other physiotherapy was applied at the days with study intervention. Walking time in the robot was individually determined i.e., a minimal walking time of 20 minutes was given, but no upper time limit, except for the length of a therapy session (60 minutes). The therapy was stopped when the patient indicated fatigue or wished to finish training. The training was started with a warming-up of 3 to 5 minutes; subsequently the walking speed was increased up to 2.0-2.5 km/h. A trained therapist supervised the training.

VR was presented to patients of the intervention group on a 42-inch screen in front of the subjects. Two VR-scenarios were used: the coin scenario, and the dog scenario 15. Both scenarios took place in a forest, where subjects had to walk along a straight alley in the middle of the screen, and solve different tasks by controlling the avatar's speed by adapting their motor activity. Patients' activity was quantified using weighted interaction torques (WIT) between the robot and the patients, which was measured at the hip and knee joints. WIT values were weighted for each step using the weighting function of Lünenburger et al [251]. The resulting WIT values were considered high if the patient performed an active movement, or low if the patient behaved passively or resisted the walking pattern of the orthosis.

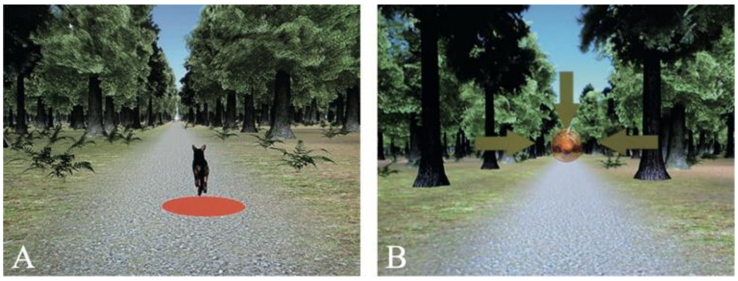


Figure 15: Virtual reality scenarios used in the study [250] A) Dog scenario: A virtual dog walking on the path displayed the desired activity level, and patients were instructed to place the red dot underneath the dog (with increasing activity, dot moved faster, and with decreasing effort, dot moved slower); B) Coin scenario: the patient has to collect coins and avoid rocks placed on the path. Patients had to increase or decrease their activity to catch or avoid the objects before they faded away.

The study found high acceptability of repetitive VR-augmented RAGT. The drop-out rate was 1/11 in the intervention and 4/14 in the control group. Patients of the intervention group spent significantly more time walking in the robot than the control group (per session and total walking time; $p<0.03$). In both groups, motivation measured with the IMI was high over the entire intervention period. The felt pressure and tension significantly decreased in the intervention group ($P<0.01$) and was significantly lower than in the control group at the last therapy session ($r=-0.66$, $P=0.005$). The Functional Ambulation Classification (FAC) is suggested as a potential primary outcome measure for a definitive RCT, as it could be assessed in all patients and showed significant response to interventions ($P<0.01$).

Held et al. [252] published a case report with the aim to (1) to investigate manipulation of the gait pattern of persons who have had a stroke based on virtual augmentation during overground walking compared to walking without AR performance feedback and (2) to investigate the usability of the AR system. They developed the ARISE (Augmented Reality for gait Impairments after StrokE) system, in which we combined a development version of HoloLens 2 smart glasses (Microsoft®) with a sensor-based motion capture system.

The ARISE system consisted of two essential components: an optical see-through head-mounted display (OST-HMD) and a sensor-based motion capture system, as shown in Figure 16. HoloLens 2 was identified as the most suitable OST-HMD, as it provides a wider field of view (43×29 degrees) compared to other devices and thus can display more virtual objects in a real-world environment. In addition, the HoloLens 2 can track head movements with an inertial measurement unit and has an intuitive hand-interaction user interface that is enabled through fully articulated hand tracking. The OST-HMD was used to visualize the AR parkour course (Figure 17 A-C). The state-of-the-art parkour course had an area of approximately 14×4 meters; it consisted of visualizations of real-life obstacles and barriers, such as blocks and floor mats, that forced the patient to perform certain leg movements. A trail of arrows indicated the walking direction, and the parkour course changed dynamically depending on the position of the patient.

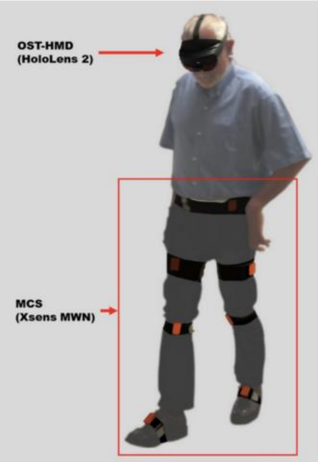


Figure 16: Patient who has had a stroke wearing the ARISE system, including the optical see-through head-mounted display (HoloLens 2) and the sensor-based motion capture system (Xsens MVN) [252]

In addition, the OST-HMD provided visual and auditive feedback based on real- time gait kinematic performance. An inertial measurement unit–based motion capture system, the Xsens MVN (Xsens Technologies B.V.), was chosen to track the kinematics of the lower limbs during gait. We strapped seven inertial measurement units on the pelvis and the lower extremity of the patient (Figure 16). The Xsens software (MVN version 2019.2) converted the rotational data from the inertial measurement units into a fully articulated virtual mannequin. This provided translational and rotational data of every large humanoid joint. With this combination, the patient was able to walk longer distances (more than 10 meters).

To increase the difficulty of the tasks the subject was asked to complete, simple math calculations were presented visually (dual task procedure, Figure 17D). The subject responded by pressing a virtual button, which was detected by the hand-tracking capabilities of the HoloLens 2. At the end of the parkour course, a knowledge of results display was shown, including the time to run the parkour course, the correct answers to the math calculations, and the percentage of time that the condition of knee flexion >45 degrees was fulfilled.

One patient with chronic minor gait impairment poststroke completed clinical gait assessments and an AR parkour course with patient-centered performance gait feedback. The participant performed a 10-meter walk test and then completed the AR parkour course three times. During walking, the 10-meter walk test and the AR parkour, the patient's lower extremity kinematics and center of mass were tracked with the motion capture system. He recognized virtual objects and ranked the usability of the ARISE system as excellent. In addition, the patient stated that the system would complement his standard gait therapy.

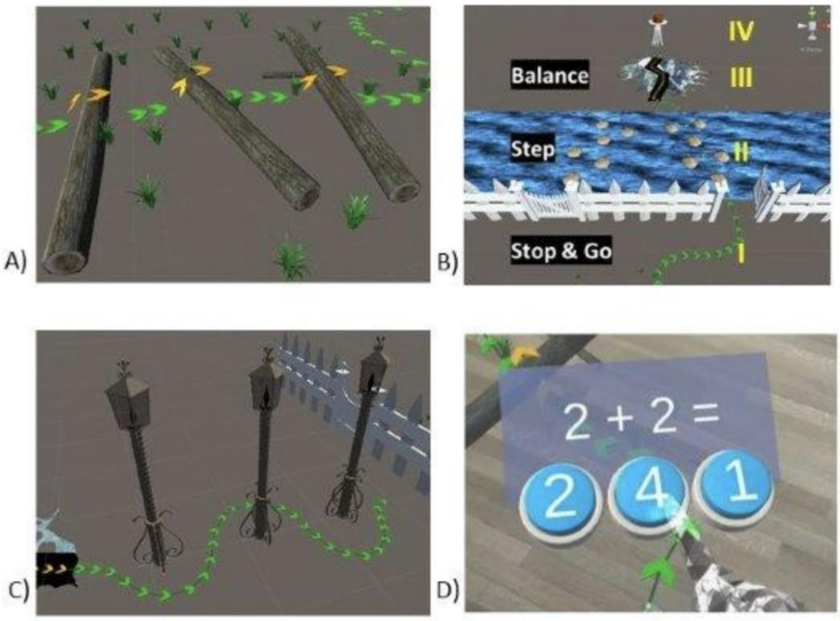


Figure 17: Augmented reality parkour course, including arrows indicating the walking direction. A) Overstep obstacle of tree trunks. B) I. Stop and go barrier; II. Stepping stones over a virtual river; III. walkable ridge-path; IV. the patient turns around and walks back.
C) Walking slalom with lamps. D) Dual-task math calculation [252]

Feng et al. [49] conducted a randomized controlled trial to investigate the effect of VR technology on balance and gait in patients with PD. The treatment group received VR training, and the control group received conventional physical therapy. Both groups received routine medication for PD. According to the patient's physical condition, the therapist conducted each treatment for 45 minutes, once a day, 5 times a week, for a total of 12 weeks. The experimental group exercise protocol was as follows:

- Warm up (5 mins): The face of the screen reaches all corners for the purpose of pulling the body for load bearing, drafting, and full range of motion.
- Game - Hands and feet touch the ball (10 mins): The ball appears in different positions on the screen, with the upper extremities and lower extremities each reaching to touch the ball for limb muscular strength, shifting the center of gravity, single leg weight, and upper and lower extremity coordination.
- Game - Hard boating (10 mins): Use your upper body to boat, while keeping balance to prevent your body from falling into the water for quick response, shifting the center of gravity, limb flexibility, and exercise adaptation.
- Game - Take the maze (10 mins): According to the situation, analyzing and selective walking in different directions until out of the maze for fast moving, body turning, and lower extremity coordination.
- Cool down (10 mins): In the original position, stretch all joints for relaxing muscles.

Individuals were assessed pre- and post-rehabilitation with the Berg Balance Scale (BBS), Timed Up and Go Test (TUGT), Third Part of Unified Parkinson's Disease Rating Scale (UPDRS3), and Functional Gait Assessment (FGA). After treatment, BBS, TUGT, and FGA scores had improved significantly in both groups ($P<0.05$). However, there was no significant difference in the UPDRS3 between the pre- and post-rehabilitation data of the control group (P>0.05). VR training resulted in significantly better performance compared with the conventional physical therapy group (P<0.05).

Choi et al. [123] conducted a randomized controlled trial to investigate the efficacy of a virtual reality rehabilitation system of wearable multi-inertial sensors to improve upper-limb function in children with brain injury. The study included children with CP or other acquired brain injury at least 12 months after onset, aged 3 to 18 years. The intervention group participated in VR training with the RAPAEL Smart Kids$^{\text{TM}}$, which was developed for rehabilitation purposes. It consists of a band-like wrist attachment with two inertial measurement unit sensors on the dorsum of the hand and distal forearm and associated software, as shown in Figure 18.

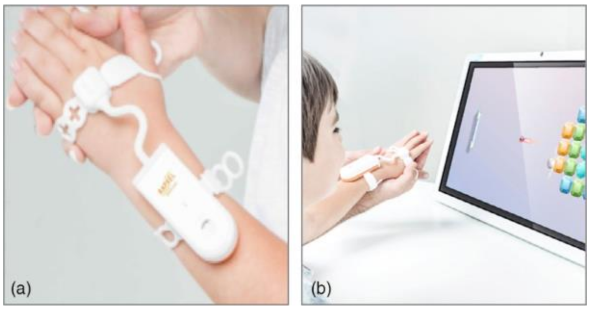


Figure 18: Component of the virtual reality device developed for upper-limb rehabilitation in children with disabilities. (a) Band-like wrist attachment device with two inertial measurement unit sensors on the hand dorsum and distal forearm. (b) Software in combination with a personal computer and a screen [123]

The virtual reality rehabilitation program consists of several games and simulations including performance of activities of daily living and facilitating motions. At the beginning of training, upper-limb capability was assessed using the virtual reality device to determine the initial difficulty level. Then, the difficulty level of the training scenarios was adjusted based on performance parameters for everyone during each training session. Simultaneous feedback was provided on a computer screen with auditory and visual feedback during and after practice. During each session with the virtual reality system, the therapist helped the child to put the device on, motivated them, and stopped them from using the opposite limb during training.

The intervention group received 30 minutes of treatment based on the virtual reality rehabilitation program, whereas the control group received conventional occupational therapy 5 days per week for 4 weeks. Furthermore, both groups received an additional 30 minutes per day of conventional occupational therapy for the affected upper limb. The amount of therapy for both groups was not different during the intervention period (1h/day, 5d/week for 4 weeks, 20h overall) but the content differed (intervention group: 30min virtual reality and 30min conventional occupational therapy; control group: two sessions of 30min conventional occupational therapy). The study reported that the virtual reality group showed more significant improvements in upper-limb dexterity functions (MA-2, virtual reality group: D=$10.09\ 10.50$; control: D=$3.65\ 6.92$), performance of activities of daily living, and forearm supination by kinematic analysis (p<0.05). In the virtual reality group, children with more severe motor impairment showed significant improvements compared to those with less severe impairment.

Rutkowski et al. [70] conducted a randomized controlled trial and compared the effects of inpatient-based rehabilitation program of patients with chronic obstructive pulmonary disease (COPD) using non-immersive virtual reality (VR) training with a traditional pulmonary rehabilitation program. The aim of this study was to determine 1) whether rehabilitation featuring both VR as well as exercise training provides benefits over exercise training (ET) alone and 2) whether rehabilitation featuring VR training instead of exercise training provides equivalent benefits.

The study recruited 106 patients with COPD to a 2-week high-intensity, five times a week intervention. Randomized into three groups, 34 patients participated in a traditional pulmonary rehabilitation program including endurance exercise training (ET), 38 patients participated in traditional pulmonary rehabilitation, including both endurance exercise training and virtual reality training (ET+VR) and 34 patients participated in pulmonary rehabilitation program including virtual reality training but no endurance exercise training (VR). The traditional pulmonary rehabilitation program consisted of fitness exercises, resistance respiratory muscle and relaxation training. Xbox 360TM and KinectTM Adventures software were used for the VR training of lower and upper body strength, endurance, trunk control and dynamic balance.

The intensity-controlled VR sessions included games provided by the KinectTM Adventures (Microsoft®). Patients participated in mini- games in which they performed certain movements in front of the motion sensor. The games included rafting, cross-country running, hitting a ball in the direction of a player on the screen, and a mountain wagon ride. Before each game, the manufacturer's instructions were displayed, indicating the goal of the game and the method of the avatar control. The therapeutic session was set individually and performed for about 20 min. During the session each patient participated in the four games in the same order in each session, 5 days a week with the same workloads. The VR training was supervised by a physiotherapist.

KinectTM training involved four games: 20,000 Leaks, Curvy Creek, Rally Ball, and Reflex Ridge. In the 20,000 Leaks game, movement tasks were focused on improving agility, dynamic balance, strengthening the lower and upper limbs and improving endurance. In the Curvy Creek game, tasks were focused on improving the elasticity of the lower body, balance and strengthening the lower limbs and improving endurance. In the Rally Ball game, tasks were focused on improving the elasticity of the upper body, strengthening the upper and lower limbs, improving the dynamic balance, and improving endurance. In the Reflex Ridge game, movement tasks were focused on improving flexibility of the upper and lower body, coordination while avoiding obstacles and improving the strength of the lower limbs, agility, balance, and endurance.

The comparison between ET and ET+VR groups showed that ET+VR group was superior to ET group in Arm Curl ($p<0.003$), Chair stand ($p<0.008$), Back scratch ($p<0.002$), Chair sit and reach ($p<0.001$), Up and go ($p<0.000$), 6-min walk test ($p<0.011$). Whereas the comparison between ET and VR groups showed that VR group was superior to ET group in Arm Curl ($p<0.000$), Chair stand ($p<0.001$), 6-min walk test ($p<0.031$). Results suggest that pulmonary rehabilitation program supplemented with VR training is beneficial intervention to improve physical fitness in patients with COPD.

Neurorehabilitation techniques using virtual reality (VR) systems have recently become widespread as a rehabilitation method for restoring phantom limb movement and alleviating phantom limb pain (PLP). However, analgesic effects have varied between studies, possibly because of differences in the characteristics of PLP between patients (e.g., cramping, burning, shooting). Osumi et al. [115] aimed to reveal the relationship between

VR effects and PLP characteristics using an exploratory factor analysis.

The movement of the intact arm and hand/fingers was detected and captured by infrared video cameras (Microsoft® Kinect™; Leap Motion). A three-dimensional computer graphic (3D-CG) figure of the patient's intact forearm and hand/fingers was visualized using 3D-CG software, then transformed symmetrically. The mirror-reversed image (i.e., the virtual phantom limb) was visually fed back to the patients via an immersive head- mounted display (Oculus Rift, Oculus VR), which could detect the patients' head angle and motion. Using the VR system, patients were able to immerse themselves into the virtual environment and control their virtual phantom limb with their intact limb movements. When participants simultaneously moved their bilateral hands, the feeling of producing intentional movements of their phantom limb was induced.

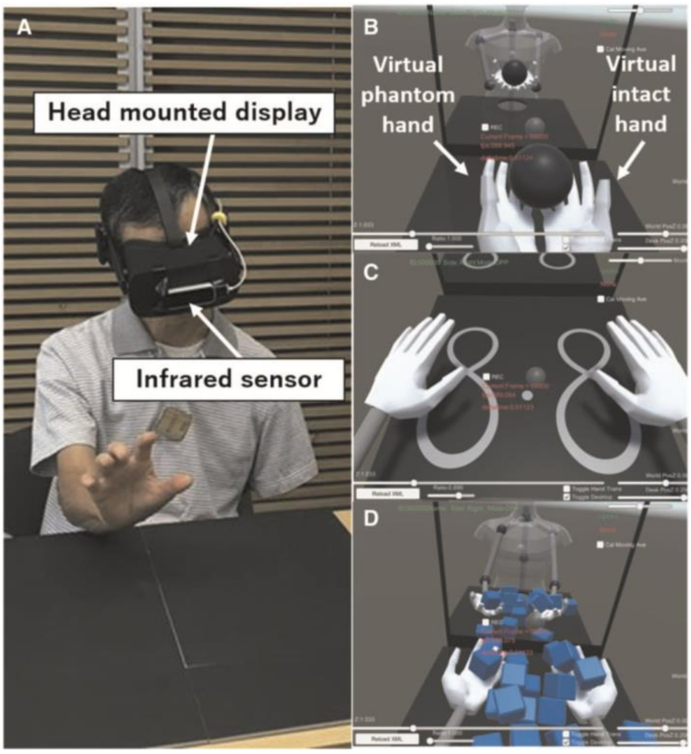


Figure 19: A) Overview of virtual reality with mirror visual feedback treatment rehabilitation setup and various tasks, as shown below. B) Putting the ball in the hall. C) Tracing figure-eight. D) Loading small blocks [115]

The short-term rehabilitation protocol comprised a single session involving three tasks, as follows: 1) Putting the ball into the hall; patients spooned and lifted the ball with bilateral hands, then carried it to the hall and finally dropped it (Figure 19B). 2) Tracing a figure-eight; patients traced a figure-eight represented in the virtual world with their virtual phantom limb at a comfortable speed (Figure 19C). 3) Loading small blocks; patients cupped small blocks with their bilateral hands and loaded as many blocks as possible (Figure 19D). Patients conducted these rehabilitation protocols for a total of 20minutes.

VR rehabilitation significantly restored movement representation ($P<0.0001$) quantified using the bimanual coupling effect and significantly alleviated PLP intensity ($P<0.0001$). The factor analysis revealed that PLP characteristics could be divided into two factors: "somatosensory-related pain characteristics" and "kinesthesia-related pain characteristics." PLP alleviation via VR rehabilitation was significantly correlated with "kinesthesia-related pain characteristics" ($r=0.47$, $P=0.02$) but not "somatosensory-related pain characteristics" ($r=0.22$, $P=0.17$).

Perioperative rehabilitation is crucial for patients receiving surgery to reduce complications and mortality. Wang et al. [136] conducted a pilot study to compare the effects of AR-based training rehabilitation programs with conventional (non-AR-based) programs considering the objective pulmonary function and subjective feasibility and potency in orthopedic patients. They developed an AR app that includes respiration training, resistance muscle training, and walking training for surgery preparation. The AR app included 10 kinds of respiration training, 34 kinds of resistance muscle training (including 6 upper limbs strengthening exercises and 28 lower limbs strengthening exercises), and walking training. These programs were designed for individuals scheduled for elective orthopedic surgery, and the patients could present with or without chronic heart failure, myocardial infarction, degenerative joint disease, or chronic obstructive pulmonary dis- ease. Healthcare providers (i.e., physiatrist, physical therapist, and nurses) were trained to choose a suitable training program for the patients.

The training program was led by an AR virtual teacher on the screen of mobile smart devices (e.g., smartphone or tablet). Patients could check the accuracy of their exercise on the screen and monitor their heart rate by wearing a specific bracelet. Meanwhile, the AR virtual teacher would recommend either an intermittent or continuous mode of walking training, and remind patients to speed up or slow down according to the results and special positions of the patient derived from the app. The AR app assisted rehabilitation in multiple modalities, including constructing interactive, entertaining, and automatic therapeutic tools for rehabilitation. In order to motivate patients to train regularly, the AR system gave incentive points according to their completeness of the pre-set program. As the incentive points accumulated, the AR virtual teacher would level up, thus inspiring the patients. Patients and physicians could receive instant feedback on the data analysis. The completeness and achievement of all the patients' training programs would be recorded in their app.

This prospective study found that pulmonary function inferred by the inspiratory flow rate was better in patients undergoing orthopedic surgery using the AR-based peri- operative rehabilitation program compared with that of the conventional program, both on the preoperative day. The perceived feasibility (levels of confidence and anxiety) and potency (cooperation and educative effect) of AR-based training were superior to conventional training, although they were not statistically significant.

Upbeat [95] is an AR-based dance game designed to improve rehabilitation therapies in upper limb amputees. The patient is instructed to follow a virtual dance instructor, performing choreographed dance movements containing hand gestures involved in upper limb rehabilitation therapy. The proposed system for rehabilitation is based on AR guidance, gesture recognition, and marker-less body tracking. A virtual dance instructor guides the patient through a set of dance movements containing specific hand gestures (Figure20). A Myo armband, worn on the forearm, is used to detect the patient's muscle activity and classify the hand gestures using detected EMG data. The patient's position is tracked with a Microsoft® KinectTM sensor and used to display a visualization of the muscle activity upon completion of the session.

The scoring system is based on the timing and accuracy of gesture completion. Each dance step shown by the virtual dance instructor contains one hand gesture that needs to be matched by the patient. Whether or not the patient successfully completes the gesture is tracked by the Myo Armband, which analyzes muscle activity to classify the movement into a recognized gesture. Performed gestures must match the one shown by the dance instructor, and should be performed within a certain time frame to be considered a correct movement. The time frame for each specific hand gesture and dance movement varies based on the choreography and music, but typically lasts between 6 and 12 seconds. The total game score is then calculated based on how many hand gestures are accurately performed by the player throughout the game.

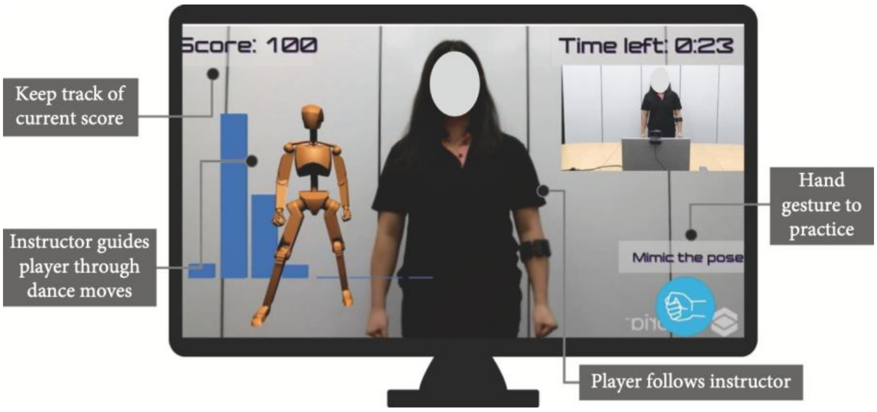


Figure 20: Upbeat’s Interface [95]

The Myo Armband contains an array of 8 bipolar surface electrodes that measure the EMG activity from the user, which is later used to produce a graph of the patient’s EMG activity. This graph is displayed upon completion of the game in the Feedback scene. Each color in the graph represents data collected by each individual sensor, and the overall analysis can be used by the practitioner to visually analyze the muscle activity patterns as an indication of the patient’s progress through the rehabilitation process. The patient’s muscle activity is then shown using an EMG graph, while a color-coded visualization of muscle activation is produced with the Mirracle AR mirror system. The postgame feedback is designed to deliver a comprehensive evaluation of the user’s performance, following methods that have proven to be effective for rehabilitation.

The recording of the patient’s performance during the game is displayed in real time on the game’s background, simulating the effect of a mirror. This setup is the most appropriate for the patients to clearly see the virtual dance instructor, as well as their own mirrored reflection (from the head to slightly above their knees), such that they could perform the dance movements with as much visual observance as possible. The authors claim that Upbeat has the potential to improve the rehabilitation process by increasing user’s excitement, giving personalized feedback, and allowing progress tracking. The portability of the system allows for rehabilitation to begin immediately after trauma, rather than waiting for prosthetics to be made or for medical-guided therapies to be concretely established.

4 Results

Table 1: Summary of Findings.

Application	Reference	Technology	Findings
Manual Dexterity	Waliño-Paniagua et al. [234]	VR (Online web page; Video Camera)	improvements in the precision of movements, execution times, and efficiency of certain functional tasks in the PPT and JTH tests in the treatment group. Although significant differences were not found in the manual dexterity between control and treatment groups, improvements were found regarding the precision and effectiveness of certain functional tasks.
	Wu et al. [235]	VR (LMC; Laptop)	Improvements in BSHS-B, QuickDASH, and iADL in the LMC group (all $p < 0.05$) compared to control group. Increased ROM of thumb IP joint and pinch strength and decrease in scar thickness over the first dorsal interossei muscle in LMC group.
	Cuesta- Gómez et al. [246]	VR (LMC-based serious games)	improvements for unilateral gross manual dexterity, fine manual dexterity, and coordination with high satisfaction and compliance.

Continued

Table 1: Summary of Findings.

Application	Reference	Technology	Findings
Upper Extremity Function	Shin et al. [233]	VR (RAPAEL Smart Glove™)	Improvements in the FMA, JTH, and SIS scores were significantly greater in the VR treatment group than in the conventional therapy group.
	Standen et al. [236]	VR (Virtual Glove)	Significantly greater change from baseline in the intervention group on midpoint Wolf Grip strength and two subscales of the final MAL.
	NeuroR [73]	Wearable marker-based AR	Results of FMA suggested a trend for greater up- per limb motor improvement in the augmented reality group (from 17% to 62%) than in the control group (from 4% to 14%)
	SleeveAR [141,237]	Wearable marker-based AR (OptiTrack Motion Capture [238])	Usability study participants gave higher assessment to the AR system.
	AR Fruit Ninja [239]	Non-wearable marker-based AR	scores higher in IG by 21%, reaching times faster by 19% and movement variability lower by 15%
	MirrARbilitation [240,241]	Marker-less AR (Microsoft® Kinect™)	exercise repetitions improved from 34.06% to 66.09%, correct exercises increased from 69.02% to 93.73%
	Colomer et al. [242]	Marker-less AR (Microsoft® Kinect™)	positive effects of the experimental intervention in both activity and participation
	Norouzi-Gheidari et al. [243]	VR (Microsoft® Kinect™) Jintronix exergame	MAL-QOM, SIS (stroke impact scale) showed a mean difference of 1.0%, 5.5%, and 6.7% be- tween the IG and CG at post-intervention.
	Elor et al. [244]	VR (HTC Vive HMD)	post-gameplay interviews using mixed 5-point. Likert Scale questions and open-ended questions. A score of 111/130 or higher was seen.
	Sánchez-Herrera- Baeza et al. [245]	VR (Oculus Rift 2 with LMC)	BBT, speed of movement, fine motor dexterity PPT, CSQ-8. Improvements in strength (p = 0.028), fine (p = 0.026 to 0.028) and gross coordination dexterity, and speed movements (p = 0.039) in the affected side were seen with excel- lent compliance and a high level of satisfaction
	Van der Meulen et al. [247]	AR (OST-HDM with haptic controller)	Good usability and engaging game, but there is still need for technical improvement regarding tracking the controller in 3D space.
	Choi et al. [123]	VR (RAPAEL Smart Kids™)	Significant improvements in upper-limb dexterity functions, performance of activities of daily living, and forearm supination especially in children with more severe motor impairment
	Upbeat [95]	VR (Microsoft® Kinect™; Myo arm-band)	Ease of use and access to aid rehabilitation im- mediately following trauma
Physical Fitness	Rutkowski et al. [70]	VR (Microsoft® Kinect™)	statistically significant improvement in the exercise performance in VR groups
	Wang et al. [136]	AR (smart mobile de-vice; wrist band)	AR app had better subjective and objective outcomes compared with a conventional model for perioperative rehabilitation.

Continued

Table 1: Summary of Findings.

Application	**Reference**	**Technology**	**Findings**
Pain Alleviation	Osumi et al. [115]	VR (Microsoft® Kinect™; Leap Motion; 3D-CG; Oculus Rift)	VR rehabilitation correlated with kinesthesia-related pain characteristics and significantly restored movement representation and alleviated PLP intensity.
Lower Extremity Function	Taesung In et al. [248]	VR Reflection Therapy	statistically significant improvements in the VRRT group compared with the control group for BBS, FRT, TUG, postural sway.
	Janeh et al. [249]	VR with GAITRite® walkway	Virtual dissociation of visual and proprioceptive signals was most promising.
	Bergmann et al. [250]	VR augmented RAGT	IG manifested positive results like high acceptability and motivation, slashed dropout rate, and an extended training period as compared to CG.
	Held et al. [252]	VR (Microsoft® HoloLens 2 Smart Glasses)	Participants ranked the usability of the ARISE system as excellent.
	Feng et al. [49]	VR	significant improvement in BBS, TUGT, and FGA scores

Abbreviations: **FMA** Fugl-Meyer Assessment Test, **JTH** Jebsen Taylor Hand Function Test, **SIS** Score Impact Scale, **MAL** Motor Activity Log, **PPT** Purdue Pegboard Test, **BBS** Berg Balance Scale, **FRT** Functional Reaching Test, **TUG** Timed Up and Go

5 Discussion

For manual dexterity, Waliño-Paniagua et al. [234] focused on MS patients and used non-immersive VR technology. Although they reported no statistical significance, they did find clinical improvements after the OT + VR intervention, with improved precision of the upper limb movements, faster performance, and a greater efficiency in the performance of certain functional tasks. They reported that although significant differences were not found between OT and OT + VR groups, the results showed a tendency towards statistical significance related to motor dexterity measured by PPT, the Jebsen-Taylor Hand Function Test and the Grooved Pegboard Test, and suggests that both approaches could be valid, and thus, complementary. Wu et al. [235] also used non-immersive VR but studied hand rehabilitation for burn victims. They posit that patients with severe hand burns who undergo leap motion training would have better improvement in ROM, scar management, and hand function. As LMC creates a natural noncontact interface for motor rehabilitation, it could provide an application in a new era of research in the field of burn rehabilitation.

Cuesta-Gómez et al. [246] claim that it is the first RCT to evaluate grip muscle strength, coordination, speed of movements, fine and gross dexterity, fatigue, and quality of life after using serious games designed for neurological diseases with the LMC system for UL rehabilitation of MS patients. They found that in the experimental group compared to the control group, results showed improvements in the post-treatment assessment for unilateral gross manual dexterity, fine manual dexterity, and coordination. These findings seemed to be more outstanding on the more affected side. Their results are in line with other studies that have employed LMC in neurological diseases.

Shin et al. [233] found clinical improvements in manipulative dexterity after a VR intervention in people with brain injury, measured using the PPT and JTT. Significant differences were however not found in the cited study among the group receiving conventional OT, leading the authors to conclude that the combination of conventional OT with VR may improve global upper limb movements. Standen et al. [236] found that despite considerable variation in their outcome measures, a significantly greater change from baseline in the intervention group was found on the Wolf Grip strength at midpoint and two subscales of the final Motor Activity Log. However, this feasibility study found that recruitment rates were so low that an impractically long recruitment period would be required to achieve the sample size indicated by the outcome measures. Moreover, training in the use of the equipment took a median of 230 minutes per patient.

NeuroR [73] presented promising results for UL motor rehabilitation, since in two case studies using the NeuroR system applied to participants that suffered a stroke more than a year ago, enhancements were observed in the motor components of the shoulder ROM and speed, measured by the evaluation instruments adopted. However, from four participants who attended the experimental group on the first case study, three demonstrated a matching of the virtual 3D arm with their actual arm. Nevertheless, one participant did not show the same reaction. He neglected the relationship between his physical arm and the virtual arm. This subject has suffered an injury in the nucleus of the thalamus and base. From neurological literature, visual stimuli were known to excite the reticular formation. Based on the tests carried out, there is evidence that participants with lesions in the reticular formation or elsewhere in the brain stem may have difficulties in stimulating motor neurons from the visual stimuli, which is a note-worthy limitation of the visual feedback mechanism used in such technologies.

SleeveAR [141,237] designed an AR system that employs multimodal feedback in its design to not only to precisely guide people in how to perform, but also to provide simple and clear awareness of the exactitude or the incorrectness of the required actions, using visual, audio and haptic cues. Although usability studies showed high assessments to the system by participants, the system is yet to be tested in a RCT setting for thorough efficacy insights. AR Fruit Ninja [239] showed that during the AR-based version of the game, as compared to PC version, scores were higher, movements were faster and more consistent, and performances were more tightly linked with arm motor function. They posit that these differences are likely due to the additional cognitive demands imposed when playing the PC-based game as the movement demands in both versions were identical. The current findings underscore how choice of human–computer interface can influence task demands and thus behavioral performances and is thus likely to be important when designing a rehabilitation protocol.

MirrARbilitation [240,241] study outcomes reinforce the idea of patient engagement during virtual rehabilitation objectively by showing an increase in the number of exercise repetitions with the use of the mirrARbilitation system, where the number of repetitions improved on average close to 50%. The system also decisive evidence on helping users perform exercises correctly following the right movement pattern. This was evidenced by the higher percentage of correct exercises with the use of the system compared to the situations without it. The system also prevented users from performing the exercises incorrectly. When using the system, the three user groups performed exercises correctly more than 70% of the time. Further studies are needed to evaluate the effects of such a system in the rehabilitation routine with clinical trials.

Similarly, Upbeat [95] designed AR system and workflow was successful at classifying hand gestures embedded in a dance routine taught by a virtual dance instructor with a success rate of 77%. Furthermore, the system was also successful in measuring EMG signals from the patient’s upper arm muscle activity, as reported by the graphical summary of the data as postgame feedback. Finally, the system was able to display a recording of the gameplay with an accurate augmentation of the musculoskeletal system overlaid over the patient’s body, allowing the visualization of the muscles being activated during each dance movement.

Most studies of mirror therapy have been on upper extremity rehabilitation, which can be explained by the way in which the mirror component was applied. Mirror therapy with a small mirror forces movements to be simple and makes it difficult to improve com- plex functions such as walking [18]. One problem with mirror therapy when used for the lower extremities is that patients must bend towards their unaffected side to look at the image in the mirror, which is counteractive to common weight support training, and this asymmetric neck posture distorts visual information and the sense of equilibrium. Taesung In et al. [248] employed VRRT to give patients task-focused training rather than simple exercises. As a result, both gait velocity and cadence increased, balance improved significantly along with range of motion and functional activity.

While most AR and VR systems for LE rehabilitation consist of stationary equipment, including a treadmill, cameras, and projection devices, AR system by Held et al. [252] enables context-specific training and can display virtual objects via the HMD in a real-world space, such as overground walking as demonstrated in the study. However, the study is limited in that it is a case report; the system requires detailed usability and feasibility study for guiding future developments. Moreover, long-term usage of such systems is required for better insight into their strengths. Feng et al. [49] also reported the between-group comparisons showed that the balance of the experimental group significantly improved relative to the control group. Since PD is a chronic progressive disease, they suggested that the visual feedback VR technique should be considered as a long-term treatment, in addition to physical therapy, to maintain gait and postural performances in PD patients.

Colomer et al. [242] reported positive effects of the experimental intervention activity and participation and influenced the progression of the participants. There was also significant improvement in timed tests related to activity after the experimental intervention, which is noteworthy as the task performance is considered an indicative of functional improvement in individuals with chronic stroke, and since movement speed and quality of movement are interrelated. It is also important to highlight that previous research on stroke survivors involving some robotic systems has shown no improvement after intervention in the Box and Block Test unless the wrist joint or finger dexterity are specifically trained. This highlights the benefits of the proposed Mixed Reality system, since it can promote hand dexterity, while being cheaper and more portable than robotic systems. Similar was the case with Bergmann et al. [250], who tested robot-assisted gait training but reported no significant improvements.

Meta-analyses examining the effect of the intensity of stroke rehabilitation on recovery suggest that the extent of recovery during the subacute stage post-stroke is related to the intensity of rehabilitation, i.e., the more time is spent in rehabilitation, the greater the extent of recovery. Norouzi-Gheidari et al. [243] reported high adherence rate to a rehabilitation intervention that supplemented ongoing rehabilitation suggests that stroke survivors in the sub-acute stage were able to participate in more rehabilitation than what rehabilitation centers are currently able to offer given financial and resource constraints. Moreover, the intervention group showed a greater level of improvement, which in some cases was statistically significant, when compared to the control group.

Elor et al. [244] designed Project Butterfly which reports on the design and evaluation of a unique VR experience paired with a soft body robotic wearable exosuit. When evaluating the baseline feasibility of PBF and CRUX in augmenting and promoting proper arm movement as defined by the established motion primitives, most users were able to complete appropriately challenging arm movements, suggesting that PBF and CRUX gave users suitable strength of their augmented arm. Additionally, the system's ease-of-use and comfort were analyzed, and most users felt that they were confident capitalizing on the therapy system. With the plethora of positional and behavioral data output produced from this VR system, there is potential to integrate machine learning protocols and AI to optimize suit controls and game difficulty to improve rehabilitation results. A set of design guidelines was also compiled for other practitioners of wearables and VR games to augment upper limb movements and motivate exercises.

Sánchez-Herrera-Baeza et al. [245] reported, despite a small sample size, several statistically significant variables showed a medium effect size. Patient satisfaction with the technology was high, and qualitative results showed good acceptance of the new treatment. Consistent with previous studies, they identified several aspects of treatment concerning patient effort, interest, feelings of pressure, and acquisition of ability in the virtual world. Van der Meulen et al. [247] also reported similarly, as their game scored high on competence, flow and positive affect, indicating that the users enjoyed playing the game, felt absorbed by the game and had the overall feeling that they were successful, skillful in completing the game. In line with this observation, Choi et al. [123] used VR system for children's rehabilitation, as they lose interest quicker and become bored easily. They also showed that virtual reality training was more effective than conventional occupational therapy in improving dexterity, performance of activities of daily living, and active forearm supination motion in children with chronic brain injury, especially those with severe motor impairments.

For physical fitness related applications, Rutkowski et al. [70] employed a VR system for training of lower and upper body strength, endurance, trunk control and dynamic balance. The study results can be considered strong due to the substantial number of patients included and the employment of control group. However, the program lasted only 2 weeks, and the authors did not evaluate the game-training satisfaction by the standardized questionnaires. Wang et al. [136] used their AR app for considering the objective pulmonary function and subjective feasibility and potency in orthopedic patients. The perceived feasibility (levels of confidence and anxiety) and potency (cooperation and educative effect) of AR-based training were superior to conventional training, although they were not statistically significant. The authors posit that the AR app could be regarded as a supplement therapy, aiding in ameliorating the rehabilitation process. The study was limited in their number of participants, and although it included subjective assessment, the study only recorded the data during hospitalization (1–2 weeks).

The advantage of VR-based technologies over conventional rehabilitation therapies has been associated with increased motivation, engagement [253], and the wide range of possible tasks/exercises that might be implemented [254]. However, it is important to understand the analgesic properties of VR and how this might interact with interventions. It is potentially beneficial, but it is also possible that patients will not have a clear understanding of the pain they are in and may push too far before they are ready. Emerging evidence has concerned the safety of using VR technology in clinical practices, especially for the rehabilitation training of patients with lower limb impairments [27,243,255]. For example, the patients may not be able to recognize their body position when using a HMD VR device, which would further lead to unexpected physical injuries [27].

Due to the above limitations, the requirement for a safer and automatic rehabilitation training tool has accumulated. In recent years, the introduction of AR into clinical applications has been proposed and verified [79–81]. AR could be a safer alternative to VR since it does not fully place the users into the simulated environment but add the fundamental elements of rehabilitation training on a real-world view [256]. In addition, compared to these interactive elements designed by VR in the virtual world, the interactive elements created by AR in the real world could induce much more embodiment to the users [80].

Moreover, due to these technological developments being recent, further re- search with medical professional involvement, a longer follow-up period and a longer intervention period are needed [250]. Cochrane review also found a significant benefit to upper-limb function with a moderate effect size when VR was used as an adjunct to usual care but not when compared to dose-controlled conventional therapy [77]. However, there was a small benefit in ADLs with VR technology, which increased to a moderate benefit when therapy was not dose-controlled. Thus, whilst VR may not be superior to conventional rehabilitation therapy, it could be a useful adjunct to increase therapy duration and intensity.

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