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Review

What Do We Know about The Use of Virtual Reality in the Rehabilitation Field? A Brief Overview

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Abstract: Over the past two decades, virtual reality technology (VRT)-based rehabilitation has been increasingly examined and applied to assist patient recovery in the physical and cognitive domains. The advantages of the use of VRT in the neurorehabilitation field consist of the possibility of training an impaired function as a way to stimulate neuron reorganization (to maximize motor learning and neuroplasticity) and restoring and regaining functions and abilities by interacting with a safe and nonthreatening yet realistic virtual reality environment (VRE). Furthermore, VREs can be tailored to patient needs and provide personalized feedback on performance. VREs may also support cognitive training and increases patient motivation and enjoyment. Despite these potential advantages, there are inconclusive data about the usefulness of VRT in neurorehabilitation settings, and some issues on feasibility and safety remain to be ascertained for some neurological populations. The present brief overview aims to summarize the available literature on VRT applications in neurorehabilitation settings, along with discussing the pros and cons of VR and introducing the practical issues for research. The available studies on VRT for rehabilitation purposes over the past two decades have been mostly preliminary and feature small sample sizes. Furthermore, the studies dealing with VRT as an assessment method are more numerous than those harnessing VRT as a training method; however, the reviewed studies show the great potential of VRT in rehabilitation. A broad application of VRT is foreseeable in the near future due to the increasing availability of low-cost VR devices and the possibility of personalizing VR settings and the use of VR at home, thus actively contributing to reducing healthcare costs and improving rehabilitation outcomes.

Keywords: virtual reality technology (VRT)-based rehabilitation; virtual reality (VR); rehabilitation; brain injury; neurophysiology

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1. Introduction

There is no unique definition of virtual reality (VR). The concept's depictions include "the use of interactive simulations to provide users with opportunities to engage in environments that appear and feel similar to real-world objects and events" [1], "an advanced form of a human-computer interface that allows the user to interact with and become immersed in a computer-generated environment in a naturalistic fashion" [2], "a range of computing technologies that present artificially generated sensory information in a form that people perceive as similar to real-world objects or events" [3], or "the use of interactive simulations created with computer hardware and software to present users with opportunities to engage in environments that appear and feel similar to real-world objects and events" [4].

Regardless of its definition, VR consists of a simulated experience of a natural or imagery environment that may or may not resemble a life-like experience. VR-based technology (VRT) consists of implementing VR using multimedia devices to allow individuals to interact with a VR environment (VRE). VR devices are essentially made of a multimedia display that provides sensory information to the user (including visual, auditory, and haptic information) and a control device that collects the user's actions (including motions, gestures, and speech). For instance, a VRT device can include motion-sensing gloves for life-like hand control (a form of VRT input) and a desktop display for showing the VRE generated by the software and the VRE interaction feedback (a VRT output, including auditory and video feedback, as well as sensory and force feedback through haptic technology).

VR needs to be distinguished from extended reality (XR), which includes augmented reality (an interactive experience of a real-world environment where the objects that reside in the real world are enhanced by computer-generated perceptual information, sometimes across multiple sensory modalities) and mixed reality (the merging of real and virtual worlds to produce new environments and visualizations, where physical and digital objects co-exist and interact in real-time). Another type of VR consists of text-based networked VR, i.e., cyberspace (that allows integrating different VR components, including sensors, signals, connections, transmissions, processors, and controllers to generate an interactive VRE that is accessible remotely).

VRT is classified according to the degree of immersion in the VRE generated by the VR device itself, including the non-immersive (traditional computer screen or tablet), semi-immersive (large 3D screen), and fully-immersive VREs (360° screens or head-mounted displays—HMDs) [5]. The degree of immersion depends on the level of isolation from the physical world that the VRE offers to the user [4]. A fully immersive VR can be achieved "by combining computers, HMDs, body tracking sensors, specialized interface devices, and real-time graphics to immerse a participant in a computer-generated simulated world that changes in a natural way with head and body motion" [6–10]. In this regard, first-person VREs using HMDs provide the participant with 3D depth perception and change the simulated view as the real-world head moves. Besides, a first-person VRE can be achieved using specially designed rooms with multiple large screens (e.g., the computer-assisted rehabilitation environment, CAREN; Motek Medical BV, Netherlands). Conversely, non-immersive or semi-immersive VR (using computers and console game systems) involves the simultaneous perception of both natural and virtual worlds [11,12]. The degree of immersion is thus a technology-related issue [1], and this critically affects the sense of embodiment, i.e., the "psychological perception of being in or existing in the VE in which one is immersed" [13,14]. Instead, this is a psychological, perceptual, and cognitive consequence of immersion, but it influences the motor-related processes [5].

A successful neurorehabilitation program needs to be intensive, repetitive, assist-as-needed, and task-oriented. VRT has been increasingly used in the neurorehabilitation field to help patients train an impaired physical and cognitive function in order to stimulate neuron reorganization (i.e., to maximize motor learning and neuroplasticity) [15–17] and restore and regain some functions and abilities. VR enables integrating physical activity into a motor task (including a game) that requires active core and body movements to control the VR experience, which aids rehabilitation training featuring intensive and repetitive issues. Indeed, a VRE allows an individual to interact with a safe and nonthreatening yet realistic environment [4], allowing moderate intensity exercises and a high degree of repetition [18]. Furthermore, VREs can be tailored to patient needs and provide personalized feedback on performance [4]. Also, VR can support cognitive training and increase a patient's motivation and enjoyment, thus potentiating rehabilitation training thanks to the fact that most exercises are task-oriented. In this regard, exercise-based games or "exergames" have become an interesting approach to support conventional rehabilitation [19]. Lastly, it is necessary to consider that VR has somewhat lower costs when compared with other advanced rehabilitation therapies (e.g., robot-assisted therapies), where it can be used independently by the patient and it is adaptable for at-home use if a telerehabilitation service is available, like that with a virtual reality rehabilitation system (VRRS; Khymeia, Italy) [20,21].

Despite these potential advantages, there are inconclusive data on the usefulness of VR in neurorehabilitation settings [18,22–26]. VR seems useful only as an adjunct to standard clinical treatment rather than as a single intervention [23–25]. Furthermore, the usefulness of VR has also been reported as limited [23,25,26]. Finally, some issues regarding feasibility and safety remain in some neurological populations [24–26]. The present brief overview aims to summarize the available literature on VR applications in neurorehabilitation settings [19,27,28], including Parkinson's disease (PD) [24,29], multiple sclerosis (MS) [30], strokes [18,31], and cognitive decline [32] while discussing the pros and cons of VR and introducing the practical issues for research.

2. Literature Data

2.1. Research Strategy

We carried out comprehensive literature searching in the Cochrane Library, PubMed, and Web of Science databases using the search term "virtual reality rehabilitation" while limited to strokes (n = 791 papers), Parkinson's disease (n = 137), multiple sclerosis (n = 73), and cognitive decline (n = 84) and duplicate papers were removed. The papers were screened according to the following inclusion criteria: clinical trials and case studies on VRT in adult rehabilitation context that were written in English. Therefore, both the authors independently reviewed all articles according to the title, abstract, and text. Articles were excluded when they either adopted extended reality, augmented reality, or mixed reality methods, were conducted in a setting not relevant to rehabilitation, did not deal with motor and cognitive behaviours, were not available in English, or belonged to grey literature, including letters, commentaries, textbook chapters, technical or theoretical descriptions, abstracts, and conference proceedings. Therefore, 11 papers for strokes, 12 for Parkinson's disease, 20 for multiple sclerosis, and 11 for cognitive decline were included in the present review. All the reviewed studies are summarized in Table 1.

2.2. Stroke

Semi-immersive (e.g., NIRVANA system; BTS Bioengineering, Milanese, Italy) or non-immersive VR devices (e.g., VRRS or the Lokomat Pro, Hocoma, Switzerland) can improve motor practice in patients after a stroke by providing multisensory feedback and promoting adaptive learning and neural plasticity. Interventions were carried out with two groups using VRT-based rehabilitation compared to conventional training for either upper limb [33,34] or lower limb rehabilitation [35–39], mainly with treadmill systems for rehabilitation [36–38]. These single data have been comprehensively assessed in three systematic reviews and meta-analyses [40–42] that pointed out that patients had better outcomes when VRT was added to conventional rehabilitation, especially when considering the Timed Up-and-Go, Berg balance scale, and anteroposterior postural sway results. It is noticeable that Timed Up-and-Go was the only mobility measure employed in the reviewed studies.

Kang et al. [36] investigated the effects of immersive VR in the context of treadmill gait for training patients with a treadmill with optic flow as compared to a treadmill and control group. They found that patients provided with a treadmill with optic flow showed a significant improvement in the Timed Up-and-Go test, 10-m walk test, and 6-minute walk test as compared to the treadmill and control groups post-treatment.

Park et al. [43] and Lee et al. [35] dealt with postural training by comparing the effects of VR-based postural control training (i.e., visual feedback by watching their actual motion) with conventional physiotherapy. The VR group only presented better results for stride length.

It has been shown that VR feedback provides an extra advantage for performance with regard to walking endurance, obstacle clearance capacity, gait velocity, and stride length when compared to a real task of evaluating stepping over real or VRE objects (for both groups) [39].

Kim et al. [38] compared VR treadmill gait training with functional electrical stimulation (FES) as compared to conventional treadmill gait training and conventional rehabilitation. The VR-FES group showed superiority in terms of the step length, walking velocity, and stride length; however, the patients that belonged to the experimental group received additional VR-based postural control training.

Another study [37] compared a VR treadmill approach (with a HMD) with simple treadmill training. The former group achieved a higher improvement in balance.

Crosbie et al. [34] provided patients with a VRE to simulate several upper limb tasks (including reaching and grasping); however, no significant changes after training were obtained. Another work [33] compared this kind of task with conventional upper limb training. The authors found significant differences in favour of the VR group for all of the outcome measures.

Gueye et al. [44] recently provided patients with upper limb VRT-based rehabilitation using Armeo (Hocoma) as compared to conventional rehabilitation. The authors found that VRT with visual biofeedback was more effective for upper extremity motor performance than conventional physiotherapy, and that this was true regardless of patient age. Clinically meaningful improvements in gross upper extremity motor function and use of the affected arm after a VT intervention were found by employing upper limb VR-based rehabilitation in a community-based stroke support group setting [45]. VRT has been also shown to be safe and effective in the acute phase after experiencing a stroke [46].

As a result, patients receiving VR showed at least some improvement in balance, mobility, range of motion, and gait performance [1,2,47–56]; however, the studies we reviewed included small sample sizes with considerable variability for the age, gender distribution, post-stroke duration, duration of intervention, frequency of intervention, duration of sessions, percentage of dropouts, and outcome measures. Only a few studies adopted a HMD for VR alongside stroke rehabilitation, showing that patients improved upper limb function (strength, precision of movement, and range of motion) with more minor compensatory trunk movements and flexion and extension of the hand and fingers [57–60]. Moreover, they found better functional recovery for gait and balance [36].

Besides, VRT has also been shown to be helpful to improve the symptomatology related to visuospatial neglect [61–64], as well as cognitive flexibility and shifting skills, selective attention/visual research, and quality of life when considering the perception of the mental and physical state [65].

2.3. Parkinson's Disease

Neurodegenerative disorders, including PD, may benefit from VRT in terms of both cognitive and motor outcomes and quality of life. We reviewed nine trials that reported on interventions concerning balance performance and balance and stepping [66–74]. These studies compared two groups (except one) [66], with one group experiencing semi-immersive VR-based rehabilitation and the other with conventional rehabilitation. A recent Cochrane review evaluated eight trials involving 263 people with PD [30]. All included studies featured small sample sizes and were largely heterogeneous concerning the study design (although commercially available VRT devices were mainly compared with physiotherapy), trial duration (between 4 and 12 weeks), and outcome measures used. Nonetheless, VR led to a moderate improvement in step and stride length compared to physiotherapy, whereas the effects on gait, balance, and quality of life were similar between the two approaches [30].

Some works [66,73–75] have pointed out that VRT is not superior to conventional rehabilitation in improving gait as a composite outcome measure, but distinct effects have been found for gait speed and stride length in terms of the superiority of VRT. The same papers investigated the effects of VRT on balance as measured by means of the Berg balance scale, Timed Up-and-Go Test, and single-leg stance test. There was no significant difference between the VR and active control interventions in improving balance as a composite outcome measure and the Berg balance scale. Other works instead reported the superiority of VR rehabilitation in determining overall improvement rather than the conventional rehabilitation programme with regard to both gait and upper limb functions [76,77].

Some other interesting but nonsignificant differences between VR and active control interventions were reported concerning global motor function as per the Unified Parkinson's Disease Rating Sale (UPDRS) part III [72–74], activities of daily living [69], quality of life as per the 39-Item Parkinson's Disease Questionnaire (PDQ-39) [67,68,72,73], and cognitive function as per the Montreal Cognitive Assessment [69].

It is noteworthy that all of the studies we reviewed included small sample sizes with considerable variability in age, gender distribution, disease duration and severity (as per Hoehn and Yahr), duration of intervention, frequency of intervention, duration of sessions, percentage of dropouts, and outcome measures. All participants were cognitively intact. Particularly, long-term outcomes were sparsely assessed in terms of exercise [70,71]. Adverse events were not reported. Exercise adherence was significantly high. Only one study adopted a HMD for VR and found slower and less rhythmic movements for individuals with PD [72]. A semi-immersive VRT study using the NIRVANA system reported on the positive effects of VR on cognitive and behavioural recovery, particularly regarding executive and visuospatial abilities compared to traditional cognitive training [78].

A fully immersive VRE provided by CAREN has been deemed necessary to achieve a more remarkable clinical improvement than that with conventional physiotherapy, particularly regarding gait velocity and stability and step width and length [79].

2.4. Cognitive Decline

VRT could be particularly effective in treating cognitive deficit in patients with different neurological disorders. A recent Cochrane review included eight RCTs involving 1183 elderly participants concerning cognitive function training [33]. All included studies featured small sample sizes and were largely heterogeneous concerning study design (albeit mainly featuring commercially available VRT devices compared with physiotherapy), trial duration (between 12 and 26 weeks), and the outcome measures used. Nonetheless, the trial results suggest a mild to moderate improvement in global cognitive function, particularly episodic memory, working memory, speed of processing and executive function, and verbal fluency, whereas no data are available for quality of life and adverse events [80–88].

On the other hand, there is some preliminary evidence for the effectiveness of VRT in training cognitive function in groups of patients with mild cognitive impairment or dementia [89–91].

Particularly, works dealing with VRT effects on cognition in patients with mild cognitive impairment or dementia have employed immersive [92–98], semi-immersive [99], and non-immersive [100,101] VR and/or virtual environments. These studies have mainly adopted cognitive training, reminiscence, and therapeutic exercises.

Hofmann et al. [99] showed that non-immersive VRT is sufficient to reduce the number of mistakes made when performing motor tasks, as well as for memory tasks [97]. VR training with VREs shown via a HMD was effective in improving attention and verbal fluency; however, similar data were obtained using a non-immersive VRE for memory training [100].

VRT can be of help for reminiscence therapy to discuss past activities, events, and experiences by using memory triggers as a potential aid [101]; however, studies have only employed mixed virtual and augmented reality [102,103] and mixed virtual reality methods [98]. Similar data are available for VR as a therapeutic tool, including a mixed-method pilot study [96]. Conversely, "exergaming" [93] in an immersive VR modality has demonstrated improved training over conventional therapy [92], also with improved arm pointing movements and one-to-one interactions than those in physiotherapist-guided training [95] while concerning the level of frailty [102]. Similar data for the superiority of an immersive VRE compared to conventional rehabilitation have been found by Montenegro and Argyriou [103] concerning object memorization and recognition, differentiating virtual vs. real sounds, and executive function and decision-making capabilities. In addition, another study [104] investigated immersive VRE effects on memory and route learning in the context of Alzheimer's disease status.

The reviewed works suffer from the same methodological limitations found for the other neurologic conditions, including small sample sizes with considerable variability in age, gender distribution, disease duration and severity (as per the MMSE or CDR), duration of intervention, frequency of intervention, duration of sessions, percentage of dropouts, and outcome measures.

2.5. Multiple Sclerosis

Given the complex clinical picture of MS, potentially involving all the systems and pathways, VRT might be a valuable tool in treating such patients. The reviewed interventions were examined with on two groups, one featuring VRT-based rehabilitation compared to conventional rehabilitation for the cognitive and motor domains, mainly using gaming through serious games and "exergames" [105,106]. Two main reviews focused on VRT-based motor benefits [31,107–109]. Consistent but explorative controlled randomized studies or pilot studies were included in these reviews, suggesting that VRT may promote functional recovery in patients with MS if coupled with robotic rehabilitation [110], improve the ability to perform daily activities [111–113], balance and gait [21,114–121], increase short-term motor learning [122], upper limb functionality [112], and processing and integration of sensory information, with a positive impact on motor and cognitive [118,123–125]; however, training differences emerged between VR-based and conventional intervention, but these were not robust when comparing VR-based intervention and passive intervention [21,108–121].

Particularly, Leocani et al. [122] highlighted the effectiveness of interactive VR rehabilitative training in improving motor learning. Patients only benefitted from "exergaming" in the studies by Jonsdottir et al. [106,107] with regard to general mental health, dual tasking and obstacle negotiation [123], and daily activities such as street crossing [111].

Concerning motor outcomes, no significant differences were observed between the VR and control groups with regard to functional balance in four studies [118,126–129]; however, opposite results were reported by other studies [54,116,117], particularly regarding upper limb motor functions [130], although with some exceptions [131]. Particularly, the entrainment of a mirror neuron system using VR feedback with a walking human avatar when providing patients with robot-aided treadmill gait training may be central for the improvement of motor rehabilitation outcomes [54]. Similarly, superior effectiveness of VR-based treadmill gait training compared to non-VR training was found concerning in terms of the overall gait performance [123] but not walking speed [115,118,120,126–128].

Concerning upper limb rehabilitation, it has been demonstrated that serious game platforms compared to "exergaming" were more useful to improve arm function, but only the "exergaming" group perceived themselves as having improved their health [106,107].

It is noteworthy that all of the studies we have reviewed have included small sample sizes with considerable variability in age, gender distribution, disease duration and severity, duration of intervention, frequency of intervention, duration of sessions, percentage of dropouts, and outcome measures. Not all of the interventions consisted of a one-to-one tailored training regime supervised by a physiotherapist [21,121]. Furthermore, some works were carried out as home-based or telerehabilitation-based interventions [20,112,119]. Besides, long-term effects were only assessed in one study [111].

Table 1. Summary of reviewed articles. Legend: BBS, Berg balance scale; CR, conventional rehab; HC, healthy control; PT, postural control exercises; TGT, treadmill gait training; TOF, treadmill walking with optic flow; TUG, Timed Up-and-Go Test; FTD, frontotemporal dementia; MDD, major depressive disorder.

		Sample (VR/CG)	Paradigm	Outcome
stroke	Kang et al., 2012 [36]	10 TOF 10 no TOF 10 CG	30 min, 5/week, 4 weeks CG1: CR CG2: CR + conventional treadmill EG: CR + TOF	Better balance and gait following TOF than CG
	Park et al., 2013 [43]	8/8	2 × 60 min, 5/week, 4 weeks CG: CR + PT (30 min, 3/week, 4 weeks EG: CR + VR-based PT (30 min, 3/week, 4 weeks)	Better stride length after VR
	Lee et al., 2014 [35]	10/11	30 min, 5/week, 4 weeks CG: CR + PT (30 min, 3/week, 4 weeks) EG: CR + VR-based PT (30 min, 3/week, 4 weeks)	Better step length, stride length, and gait velocity after VR; no effects for TUG and BBS
	Jaffe et al., 2004 [39]	10/10	60 min, 3/week, 2 weeks CG: real stepping EG: VR stepping	Better velocity, stride length, obstacle clearance capacity, and walking endurance after VR
	Kim et al., 2012 [38]	9 VR + FES 9 FES 9 CG	30 min, 5/week, 8 weeks + TGT (20 min, 3/week, 8 weeks FES: CR + TGT + FES (20 min, 3/week, 8 weeks) VR-FES: CR + TGT + VR-FES (20 min, 3/week, 8 weeks)	Better muscle strength after VR-FES and FES Better gait speed after VR-FES Better BBS in all groups
	Jung et al., 2012 [37]	11/10	CG: TGT (30 min, 5/week, 3 weeks) EG: VR-based TGT (30 min, 5/week, 3 weeks)	Better TUG and ABC after VR-TGT
	Crosbie et al., 2012 [34]	9/9	CG: CR (reach to target, reach and grasp), 30–45 min, 3/week, 3 weeks) EG: upper limb VR tasks 30–45 min, 3/week, 3 weeks	No difference
	Ögün et al., 2019 [33]	33/32	CG: CR (gripping and handling) 45 min, 3/week, 6 weeks + passive VR therapy (15 min, 3/week, 6 weeks) EG: upper limb VR tasks, 60 min, 3/week, 6 weeks	Better FMUE, ARAT, FIM, and PASS after VR
	Gueye et al., 2021 [44]	25/25	45min, 4/week, 3 weeks CG: CR EG: Armeo training	Better FMUE, FIM, and MoCA after VR
	Johnson et al., 2020 [45]	30/30	45 min, 2/week, 8 weeks CG: CR EG: upper limb VR training	Better FMUE after VR
	Lin et al., 2020 [46]	38/114	45 min, 2/week, 8 weeks CG: CR EG: CR + VR training (15min, 2/day)	better upper limb muscle strength, depression, and anxiety scores; no difference in the functional status

Table 1. *Cont.*

		Sample (VR/CG)	Paradigm	Outcome
Parkinson's disease	Lee et al., 2015 [66]	10/10	CR: neurodevelopment treatment + FES 30 min, 5/week, 6 weeks EG: CR + VR dance exercise (30 min)	Better BBS after VR
	Yang et al., 2015 [72]	11/12	50 min, 2/week, 6 weeks CG: PT EG: VR-based PT	Better BBS after VR
	Yen et al., 2011 [73]	14 +VR 14 −VR 14 CG	30 min, 2/week, 6 weeks CG1: PT CG2: CR EG: VR-based PT	Better equilibrium scores, verbal reaction time after VR
	Liao et al., 2015 [67]	12 VR 12 active CG 12 passive CG	45 min, 2/week, 6 weeks EG: balance board therapy + TGT (15min) CG1: CR CG2: fall prevention education	Better obstacle-crossing performance, dynamic balance, TUG after VR
	Pedreira et al., 2013 [68]	22/22	50 min, 3/week,4 weeks EG: Nintendo Wii therapy CG: CR	Better UPDRS and PDQ-39 after VR
	Pompeu et al., 2012 [69]	16/16	30 min, 2/week, 7 weeks CG: CR EG: CR + 30min Nintendo Wii therapy	Better UPDRS-II after VR
	Shen et al., 2014 [70]	26/25	3/week, 4 weeks in lab, then 5/week, 4 weeks at home, then 3/week, 4 weeks in lab EG: lab (15 min VR dancing, 15 min VR-PT, 30 min TGT), home (20 min fall-prone activities CG: lab (60 min) home (20 min) of stepping and walking exercises	Better balance, fall rate after VR
	van den Heuvel et al., 2014 [71]	17/16	60 min, 2/week, 5 weeks EG: balance board therapy CG: PT	Better Functional Reach Test after VR
	Pazzaglia et al., 2020 [75]	26/25	40 min, 3/week, 6 weeks EG: VR therapy CG: CR	Better BBS and overall gait performance after VR
	Cikajilo and Potisk, 2019 [76]	10/10	30 min, 3/week, 3 weeks EG: immersive VR therapy CG: non-immersive VR therapy	Better upper limb function after immersive VR therapy
	Feng et al., 2019	14/14	45 min, 5/week, 12 weeks EG: VR-based gait training CG: CR	Better balance and gait (BBS, TUG, UPDRS III after VR
	Santos et al., 2019 [74]	15/15 + 15	50 min, 2/week, 8 weeks EG: VR + CR CG: VR therapy CG: CR	No significant differences

Table 1. *Cont.*

		Sample (VR/CG)	Paradigm	Outcome
Cognitive decline	Bourrelier et al., 2016 [91]	7 MCI 17 HC	40 min Immersive harvesting-fruit scenario Physiotherapist-led exercise session	Preferred VR experience
	Eisapour et al., 2018 [92]	6 dementia	20 min, 5/week, 1 week Therapist-guided exercise Immersive VR farm environment Immersive VR gym environment	No difference
	Manera et al., 2016 [93]	10 dementia 10 HC	VR forest 15 min	Better mood but higher fear/anxiety after VR
	Mendez et al., 2015 [94]	5 FTD	Conference table immersive virtual environment	Better social-emotional behaviour after VR
	Moyle et al., 2018 [95]	10 dementia 10 HC	VR forest 15 min	Better mood but higher fear/anxiety
	Optale et al., 2010 [96]	36 MCI	VR memory training 2/week, 12 weeks	Better cognitive outcome after VR
	Siriaraya et al., 2014 [97]	20 dementia 8 HC	Reminiscence room Virtual river and park tours Gardening	Preferred VR experience
	Aruanno et al., 2017 [98]	11 AD	15 min Short-term memory activity Memory game Memory game with spatial mapping	Preferred VR experience
	Hofmann et al., 2003 [99]	9 AD 9 MDD 10 HC	VR shopping route 3/week, 12 weeks	Preferred VR experience
	Man et al., 2012 [100]	20/24 MCI	30 min, 2–3/week EG: non-immersive VR memory-training CG: therapist-led memory training sessions	Better memory task after VR
	Karssemeijer et al., 2019 [102]	38/38 + 38 dementia	30 min, 3/week, 12 weeks EG: exergame training CG: aerobic training CG: active control intervention	Better level of frailty after VR

Table 1. *Cont.*

		Sample (VR/CG)	Paradigm	Outcome
Multiple sclerosis	Russo et al., 2018 [110]	23/21	EG: RAGT + VR CG RAGR-VR	Better gait performance after RAGT + VR
	Stratton et al., 2015 [111]	26/19	EG: VR daily activities CG: CR daily activities	better performance of daily activities after VR
	Robinson et al., 2015 [121]	56/–	Balance board therapy	Better balance and gait after VR
	Gutiérrez et al., 2013 [118]	25/25	EG: at home balance board therapy (20 min, 4/week, 10 weeks) CG: CR (40 min, 2/week, 10 weeks)	Better BBS and TUG after VR training
	Kramer et al., 2014 [120]	70/–	Balance board therapy	Better balance and gait after VR
	Eftekharsadat et al., 2015 [117]	30/–	Balance board therapy	Better balance and gait after VR
	Thomas et al., 2014 [112]	30/–	At home balance board therapy	Better balance and gait after VR
	Thomas S et al., 2017 [113]	30/–	Mii-vitaliSe testing	Preferred VR experience
	Leocani L et al., 2007 [122]	12/–	VR-aided short-term motor learning	Better performance
	Jonsdottir J et al., 2017 [107]	10/6	EG: VR upper limb motor tasks CG: CR upper limb motor tasks	Better performance after VR
	Gutierrez et al., 2013 [118]	25/25	EG: VR sensorimotor tasks CG: CR sensorimotor tasks	Better performance after VR
	Kalron et al., 2016 [119]	16/16	EG: CAREN CG: PT	Better balance and gait after VR
	Peruzzi et al., 2016 [123]	8/–	VR-based dual tasking and obstacle negotiation	Better performance after VR
	Prosperini et al., 2013 [20]	36/–	At home balance board therapy	Better balance and gait after VR
	Brichetto G et al., 2013 [116]	36/–	Balance board therapy	Better balance and gait after VR
	Calabrò et al., 2017 [114]	34/–	EG: RAGT + VR CG RAGR-VR	Better balance and gait after VR
	Molhemi et al., 2021 [129]	19/20	45 min, 3/week, 6 weeks EG: exergames using Kinect CG: conventional balance exercises	No significant differences but falls and overall cognitive-motor function
	Cuesta-Gómez et al., 2020 [130]	15/15	60 min, 2/week, 10 weeks EG: serious Games for the upper limb (15 min) + CR (45 min) CG: CR (60 min)	Better unilateral gross manual dexterity, fine manual dexterity, and coordination following VR
	Waliño-Paniagua et al., 2019 [131]	13/13	30 min, 2/week, 3 weeks EG: occupational therapy + VR games CG: conventional balance exercises	No significant differences in manual dexterity
	Lamargue-Hamel et al., 2015 [124]	30/–	Cognitive impairment assessment	VR assessments are promising in identifying cognitive impairment in MS

3. Discussion

3.1. Potential Advantages and Side Effects of VR Rehabilitation

Overall, the available data in the literature do not fully support the effectiveness of VR exercise when compared to traditional training methods. There are inconclusive data regarding the usefulness of VR in neurorehabilitation settings, mainly owing to methodological discrepancies (with particular regard to sample size, randomization, blinding, control groups, trial duration, compared devices, and outcome measures), especially concerning cognitive rehabilitation [18,23–27]. VR seems valuable and practical only as an adjunct to standard clinical treatment rather than as a single intervention [18,23–27]. Furthermore, some reports have rated the usefulness of VRT as limited [18,23–27]. Finally, some issues regarding feasibility and safety remain for the neurological population [18,23–27].

It seems reasonable to forecast that immersive VRT will add several benefits in addition to conventional rehabilitation training [18,23–27]. There is evidence that these approaches may provide patients with more interesting, motivating, and persistent motor practice and permit patients to be trained in activities that may be dangerous if practiced in a real-world setting (e.g., driving). Indeed, performing a task that may be now too difficult, time-consuming, or impossible to do in a natural world setting is instead feasible when using VR. Furthermore, VRT enables therapists to provide standardized rehabilitation protocols, controlled stimulus presentations, and objective clinical progress and performance measures. VREs can be tailored to patient needs and provide personalized feedback on performance [4]. Lastly, it is necessary to consider that many VR devices have somewhat lower costs than other advanced rehabilitation therapies (e.g., robot-assisted therapies), can be used independently by the patient, and are adaptable for at-home use if a telerehabilitation service is available [21,22].

Notwithstanding these potential advantages, there are some possible side effects of VR that must be kept into account. First, simulator sickness is a kind of motion sickness experienced by people in motion or vehicle simulations. This syndrome is characterized by discomfort, fatigue, nausea, and disorientation. It arises from the discrepancy between a more vigorous motion perceived by vision and hearing and a weaker motion perceived by the vestibular system and proprioception, which leads to simulator sickness. The frequency and severity of simulator sickness depend on the device (HMD vs. non-wearable displays), the type of tasks (e.g., walking vs. driving), and the individual's clinical and demographical features. In this regard, some fear new devices or are very sensitive to simulated environments. This may even induce persecutory delusion and paranoia in schizophrenia patients.

Conversely, reducing anxiety symptoms has been reported following fully immersive VR treatment (e.g., using CAREN) [132,133]. Furthermore, VR practice may cause lasting motion sickness, so it is necessary to take care of the patients during and after treatment. Besides, VR may induce eyestrain-related issues such as eye fatigue and discomfort, dryness and redness, and reduced visual acuity, which falls under computer vision syndrome [133,134]. These findings are more frequent when using HMDs, but this significantly depends on the given display characteristics [132,133]. All these factors need to be considered carefully when considering VRT-based rehabilitation [132,133].

3.2. Issues for Research

There are still some new or partially explored issues in VRT implementation in the neurorehabilitation field. Importantly, we have to consider the opportunity to adopt HMDs vs. standard displays. The former allows generating better immersion and life-like experiences due to the 3D depth perception achieved via binocular discrepancy and a dynamic field of view with the use of head tracking systems; however, such VR devices can be particularly expensive (e.g., HMDs and 360° VRT devices), non-available in every rehabilitation centre, sometimes challenging to wear and deal with, and can yield significant ocular disturbances.

The neurophysiological basis for the use of VRT to foster motor and cognitive function recovery still requires elucidation. Indeed, it has been proposed that VR yields a reshaping of frontoparietal connectivity in the alpha and theta frequency range. This may be extended to all the neuropsychiatric and neurocognitive disorders that share a connectivity breakdown within frontoparietal networks.

There is a particular population who may benefit from VRT to alleviate both patient and physiotherapist burden, including patients in an intensive care unit, those in a minimally conscious state, and those suffering from a severe traumatic brain injury. The positive effects of VRE may also be found regarding cognitive impairment in patients with muscle diseases, which is an unexplored issue. All these populations are very frail and feature severely limited functional communication capacities. Although preliminary, the data shown in the literature suggest that VRT may help increase communication and facilitate the delivery of a rehabilitation service.

Another population that likely requires high care for physical, psychological, and cognitive rehabilitation is the post-COVID-19 population. Owing to the unfortunately growing number of cases and consequent healthcare system burden, VRT may facilitate the delivery of fast and tailor-made rehabilitation at a distance [134].

Lastly, definite cost–benefit analysis is still missing, and although the cost of VR devices has dropped significantly, the software and hardware management required is still highly demanding, with particular regard to customized VREs. Therefore, tailored rehabilitation planning is always mandatory to better manage individuals and optimize resource allocation.

4. Conclusions

The available studies on VRT for rehabilitation purposes from the past two decades are primarily preliminary and feature small sample sizes. Furthermore, the studies dealing with VRT as an assessment method are more numerous than those harnessing VRT as a training method; however, the reviewed studies show the great potential of VRT in rehabilitation. The comprehensive application of VRT is foreseeable shortly due to the increasing availability of low-cost VR devices and the possibility of personalizing VR settings and delivering VR at home, thus actively contributing to reducing healthcare costs and improving rehabilitation outcomes through tailored rehabilitation at a distance.

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