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NEUROREHABILITATION USING VIRTUAL REALITY FOR POST-STROKE PATIENTS: MEDICAL UTILITY AND ETHICAL ASPECTS

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Abstract: Stroke is a leading cause of disability amongst adults worldwide. While mortality rates decreased in the last decades, the morbidity associated with the occurrence of stroke is a major cause of disability, missed days of work, decreased quality of life and of increased healthcare costs. Stroke survivors frequently suffer from speech impairments, motor deficits, spasticity, cognitive impairment or bowel and bladder dysfunction. Rehabilitation interventions can aid in alleviating the impact these complications have on the activities of daily living, improving cognition, gait and balance, decreasing spasticity and reducing pain. While classic rehabilitation programs were proved to be highly efficient in achieving these goals, the implication of newly developed technologies such as virtual reality (VR), when available, could improve patient outcomes, providing an easy-to-use, exciting new tool that can be used both in a clinical setting and at home.

In this paper, we review how VR has emerged as a highly promising tool in post-stroke comprehensive rehabilitation programs, and we escalate the most recent progress in the field while emphasizing the ethical aspects regarding the use of VR in post-stroke neurorehabilitation.

Keywords: stroke, rehabilitation, disability, spasticity, virtual reality, ethics.

INTRODUCTION

Stroke is a leading cause of disability and death in the adult population, with over 13 million new cases worldwide each year according to the World Stroke Organization (WSO) [1]. While stroke can occur in all stages of life, the risk increases with age. According to WSO, approximately 40% of all strokes occur in patients over the age of 70 compared to 8% in patients under 44 years of age [1]. The overall incidence of stroke decreased in the last decade, but it seems the prevalence rates have increased in the under 50-year-old age groups, making the development of new rehabilitation strategies even more necessary [1]. Stroke mortality has also decreased in the last decades, but the disease is still associated with high morbidity. The most frequent post-stroke sequelae are motor impairment, spasticity, speech impairment, dysphagia, memory and cognitive deficits and bowel and bladder dysfunctions [2-4]. Approximately 50% of stroke survivors are left with various degrees of impairment of arm function [5]. These disabilities lead to elevated healthcare costs, missed days of work and decreased quality of life [6]. Although classic rehabilitation programs are highly efficient for treating stroke patients, developing new protocols using the latest technologies available, such as virtual reality (VR), could help improve the results and offer patients a more relaxing environment during their recovery. VR is a newly developed computer-based tool that enables users to interact with a simulated environment [7]. The visual image is provided through a computer screen or special VR glasses, while the

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sound is generated in headphones or speakers. Some of the more advanced VR technology can also provide the user with tactile information through haptic feedback tools [7].

VR is beginning to be used for a variety of medical rehabilitation therapies. VR headsets (HMD) have been trialled for patients suffering from Parkinson's disease, to improve their gait pattern [8] and for children with cerebral palsy to operate motorized wheelchairs [9] and enhance their spatial awareness [10]. Several VR-based approaches have also been investigated for stroke rehabilitation, assessing either the rehabilitation of the upper limb, cognitive improvement, gait and balance interventions or the rehabilitation of both upper and lower limbs [11]. Some studies conducted on small groups of patients showed that VR systems used for the rehabilitation of the upper limb after a stroke were able to improve the function of the upper arm and the activities of daily living (ADL) [7, 12, 13]. The effects of VR were demonstrated to be similar on the lower extremities and balance [14-16].

Augmented reality (AR) seems to catch up with VR in this respect, as well. AR provides a composite view, overlapping computer-generated items on the real environment the user sees. A study found that cognitively healthy participants experience an increased sense of presence in VR environments and higher speed in tasks performing, but AR produced more individual excitement and activation than VR [17]. There is still a great deal of incongruence between the findings of small studies regarding the comparison of efficacy between VR and classical rehabilitation. Some studies found VR to be superior to conventional physical treatment [9], whilst others found no superiority [18].

Classical approach in stroke rehabilitation

Rehabilitation is crucial in helping stroke survivors to gain the highest level of independence possible. Each patient should benefit from a personalized rehabilitation plan that tackles their individual needs such as alleviating spasticity and pain, speech improvement, gait and balance reeducation and motor function recovery. Furthermore, many patients also suffer from urinary tract infections due to bladder dysfunction, anxiety and depression which also have to be addressed to achieve good results during rehabilitation.

The neurobiological mechanisms implicated in stroke rehabilitation include brain plasticity, the brain reward system and the mirror neuron system [19]. Brain plasticity manifests itself through the potential of an injured cortex to rewire and reorganize itself [20, 21]. For example, at the onset of hemiparesis, the cortical representation of the affected limb is suppressed, leading to further inhibition of its spontaneous use [20]. Intensive, repetitive and task-specific exercises are essential principles both in the current stroke neurorehabilitation practice and in the newer VR technology, which are used to harvest the brain's potential to relearn, readjust and eventually improve its function [21, 22]. Rewards, such as scores, acknowledgment of performance, or financial incentives, by stimulating the mid-brain dopaminergic system, enhance brain plasticity and the retention of motor learning [23]. Furthermore, functional MRI studies have revealed an increase in contralateral activation and a decrease in the ipsilateral activation of the cortex following intensive practice, together with the representation on the screen of the specific activities, as a result of long-term potentiation that strengthens the result and the mirror neuron system [24-26]. Mirror neurons are both active in self-processing, enabling action observation, and in other-processing, enabling imitative learning [27]. Additionally, it has been suggested that learning by imitation could also facilitate the reorganization of the gray matter through similar mechanisms to the ones described above [28].

The recovery after a stroke is heterogenous good results were proven to be associated with high engagement and motivation in both the patient and his family [29].

There are numerous physiotherapy interventions available at this time, their main focus being the improvement of balance, movement and gait. Either based solely on the interaction between the patient and the physiotherapist, or assisted by electromechanical devices, these techniques were proved to be highly efficient in improving motor function in stroke patients [29, 30].

Another important aspect of stroke rehabilitation is the management of spasticity. However, physicians have to keep in mind that treating spasticity is not always necessary, as it might decrease functional performance of the patient [31]. When indicated, the alleviation of spasticity can be best achieved by combining both pharmacologic and nonpharmacologic treatments. The scope of treating spasticity is to decrease pain and discomfort, correct abnormal limb postures, improve functional movements, ease the burden of the caregiver when performing actions like dressing the patient and also, to lower the risk of pressure ulcers [31, 32]. Some of the therapies that address spasticity are physiotherapy [31], antispasmodic oral medication [33], intramuscular injections with botulinum toxin (BT) [34-36], non-pharmacological interventions such as repetitive peripheral magnetic stimulation for improving functional ability and activities of daily living [37, 38], and even surgical treatments [39].

Furthermore, numerous devices can be used in order to ease the patient's disability, such as: (i)Ankle-foot orthosis, in case the patient suffers from foot drop consequent to stroke, which was proved to significantly improve walking impairment, walking activity and balance [40]; (ii) Shoulder joint functional orthosis for patients suffering from shoulder joint subluxation, which was found to prevent the development of shoulder-hand syndrome in hemiplegic post stroke patients [41]; (iii) Walking aids like canes, walking frames, crutches, that were proved to improve balance, stability during walking. However, their involvement in decreasing the risk of falling is still disputed [42, 43].

Although classic rehabilitation therapy was proved to be beneficial to the recovery of patients after stroke, there is always need for new strategies that could improve its outcomes and the adherence of patients to therapy.

The use of VR in stroke rehabilitation, past and present

VR refers to computer-generated simulations of real environments. The use of navigational VR environments leads to the acquisition of new skills and improved cognition in daily living activities [44]. VR approaches may address perception through one sensing system (sight, hearing, touch, olfaction) or more at the same time and allows users to act upon the virtual environment. Depending on the degree the user is isolated from stimuli from the real environment, VR provides different degrees of immersion. Non-immersive non-interactive VR appeared once with screen projections and images generated on a display and with sound rendering through technological means. Immersive VR emerged in the 1950s with the first head-mounted display system (HMD) invented in 1968. It started to become popular in the 1980s and by the 1990s, NASA and the United States military were using VR for training their personnel. The mass production of VR devices also started in the 1990s and ever since the technology has gained attention from various fields of work [45]. New approaches in this direction include semi-immersive VR and augmented reality. Healthcare is one such field where VR was found to bring multiple benefits, from medical training to marketing and nevertheless to patient treatments [46].

The technology behind VR-assisted stroke rehabilitation has seen continuous development in the past several decades. The early systems used complex and expensive hardware devices that could not be used outside a dedicated laboratory, therefore making them unsuitable for current practice [47]. At the beginning of the 2000s, VR technology started to become more accessible, laying the groundwork for the majority of systems that are used by rehabilitation specialists nowadays [48]. Amongst the first technologies to be utilized were the robotic devices in a virtual environment [49-52]. The most important advantage they possessed was the possibility of adjusting the parameters, such as intensity of training and feedback, in order to individualize the session and consequently to obtain the best possible outcome [53]. One example of such system consisted of a PC workstation and two types of gloves, the CyberGlove and the RMII Glove, each of them being more suited for specific hand rehabilitation exercises (force exertion training in the case of the RMII Glove and fine motor skills training in the case of CyberGlove) [53]. This type of system was called non-immersive. Later on, the camera-based VR technology, also known as immersive because of the sense of presence it gave to the user, started to gain more traction. After the launch of the Nintendo Wii console (Nintendo, Redmond, Washington) in 2006, scientists began exploring the options to using it both as an alternative and as a complementary method for stroke rehabilitation [54, 55]. In 2010, Microsoft Kinect (Microsoft Inc., Redmond, Washington) emerged, bringing the potential of VR use in stroke rehabilitation once again into the spotlight. The PlayStation EyeToy (Sony Computer Entertainment America LLC, San Mateo, California) was also considered and used in several studies [56]. Examples of immersive VR systems that are well-established include IREX (GestureTek, Toronto, Canada), PHANToM (SensAble Technologies Inc., Woburn, Massachusetts) and others. An interesting approach is the Computerized Augmented Reality Environment (CAREN), providing users with a 360-degree projection in a spherical dome, adding floor movements and inclination in accord with the interactive experience provided by visual stimuli and user actions. CAREN is useful in reducing physical and cognitive impairments [57], but also in improving neuropsychiatric symptomatology [58].

3a. Non-immersive VR

VR systems vary from non-immersive to immersive, depending on the degree of interaction and envelopment with the simulated environments. Non-immersive VR allows minimal interaction with the virtual environment on a device screen (such as PC, smartphone or tablet) via a mouse, a joystick or an interactive display or projection. In non-immersive VR, the user is only an external observer, because the content on the screen can be seen based only on how the device is held or moved. Even though the interaction with the environment is limited, non-immersive VR training experience is more captivating and entertaining than conventional therapy, reducing the sense of fatigue, boredom and drudgery arising from repetitive tasks [59]. Some studies have shown that, for patients suffering from mild to moderate upper limb motor impairment after stroke, non-immersive VR is as effective as widely available recreational activities when used as an add-on to conventional therapy [18].

If used as an alternative to conventional rehabilitation therapy, non-immersive VR could provide stroke survivors with autonomy, enhanced participation and a more personalized approach to rehabilitation programs [60]. Non-immersive VR is relatively inexpensive, easy to use and widely available as commercial computer games, hence it could mitigate the burden on the global healthcare systems created by the scarcity of skilled personnel and financial resources needed for the implementation of conventional rehabilitation programs.

3b. Immersive VR

When VR is provided through a head-mounted display (HMD), the interactivity gives the user an extensive sense of being immersed in a virtual environment as if it were a real complete environment. Such immersive VR using HMD has been shown in small studies to be efficient in rehabilitating the upper limb in both acute and chronic stroke patients [2, 61].
Stroke survivors left with paresis of the upper limb tend to engage in a 'learned no-use' behaviour, using only the unaffected limb to the detriment of the recovery of the affected limb [62, 63]. Conventional therapies, such as mirror therapy and constraint-induced movement therapy, seek to encourage the patient to 're-learn' to use the affected limb. Immersive VR facilitates task performance in the same manner as the mechanisms behind these conventional methods, helping the patient to overcome the 'learned no-use' behaviour [61]. It provides visual feedback of the movement of the affected limb, similar to the conventional mirror therapy that entails that a mirror, placed between arms or legs, reflects the moving non-affected limb and gives the illusion of movement in the affected limb [64]. However, in immersive VR, participants perceive that the movement of their affected limb is at a higher degree than in real life, encouraging future use of the limb. Interestingly, this effect is maintained long-term, impacting positively the future recovery of the affected areas [65]. Another traditional way of encouraging movement in the affected limb is to apply a restriction on the movement in the non-affected limb and compel the patient to use the affected limb instead. The advantage of immersive VR is that encourages the patient to use the affected limb without the need to constrain the unaffected side, so the patient can move freely both hands. At the base of the positive effects of reversing the 'learned no-use' behaviour sits the quality of fully immersive VR to help the user to focus entirely on the given task. It may therefore also help compensate for poor deficits in attention, which are common neuropsychological problems after stroke [66].

4. Efficiency of VR-based rehabilitation intervention in stroke

Lately, efforts are made to provide scientific evidence of higher methodological quality regarding the impact of VR-based rehabilitation interventions in stroke.

The most recent Cochrane systematic review regarding this aspect, published in 2017, included 72 small sample size studies, providing low-quality evidence that VR was not better than conventional therapy in improving post-stroke users' ability to use their upper limb or their walking speed, but provided slightly more improvements in the ability to perform activities of daily living than usual interventions (the remanence of this effect in time was not tested). Mild adverse effects like dizziness, pain and headache were reported [7].

But a 2019 systematic review presenting also a meta-analysis of research results regarding the VR-based training effect on function in chronic stroke patients, shows a moderate size effect of VR rehabilitation interventions on upper limb and lower limb functional outcomes. For this population, a VR-based rehabilitation program must cover 8 weeks to be efficient. Programs based on sessions provided occasionally seem to be more effective than programs based on daily sessions [67].

A 2019 review provides evidence that VR-based rehabilitation can generate significant improvements in most cognitive domains (executive and visual-spatial orientation, speech, attention, and memory) through motivation and improved participation [68]. Another systematic review with meta-analysis, published in 2021, states that VR-based training significantly improves memory, executive functions, and visual-spatial orientation when compared with conventional interventions. No significant differences between the two approaches were found regarding global cognitive functioning, attention, verbal fluency, depression and quality of life [69].

Anyway, there are still important differences between the results of different studies, in regarding the benefits of VR-based rehabilitation in post-stroke population, when compared with conventional therapy [70]. Clinical reasoning must be used when deciding the optimal approach, in a personalized manner, in terms of VR/conventional intervention, as well as in terms of complexity, intensity, frequency and duration of sessions and the overall rehabilitation program.

5. Advantages and limitations for VR in stroke rehabilitation

The studies using VR for rehabilitating stroke patients have revealed both its advantages and limitations. VR technology now offers easy portability and the possibility of implementing well-known concepts of rehabilitation programs (task-specific, repetitive and high-intensity) from home, thus allowing the patient more time to focus on the exercises.

The main advantage of VR technology is that it offers the opportunity for interactive behavior with a naturalistic environment simultaneously with the monitoring, recording and assessing of this behavior. The system is able to provide user quantified feedback in real-time regarding the level of performance in tasks. The VR-based system scan automatically adapts the intensity and complexity of the experience to every individual case [71, 72]. Regarding this particular aspect, it is important to note that immersive VR has been demonstrated to be superior to non-immersive VR in is as effective as widely available recreational activities, several studies showing improved results in FIM (functional independence measure), TUG (timed up and go) and 10MWT (10-meter walk) tests after using these technologies [47, 73-75]. The clinician can also access the feedback, therefore being able to track the progress of every patient and change the settings accordingly [76]. Furthermore, patients have reported a more enjoyable experience when using VR technology in comparison to traditional therapy and as a result, they were experiencing enhanced motivation and willingness to do more repetitions [77]. Enhanced motivation has also been shown to be promoted by the integrated game features existent in most VR rehabilitation systems. Gamification provides a more engaging approach than conventional rehabilitation interventions, and offers user diverse and complex tasks and attainable objectives. VR-based interventions are supported by advanced ICT technology, also provide real-time feedback on user's performance and endow researchers and clinicians with important assessment tools, empowering them to quantify the progress of the patients and research participants and thus, providing scientific evidence regarding the benefits of differently designed intervention on very specific aspects of functioning, activity and participation [78].

Finally, yet importantly, VR allows people to practice unsafe activities, such as crossing the street, without any associated risk [76]. VR-based rehabilitation could be especially beneficial for people that are restricted by their location, financial means or that are homebound or reliant on different types of caregivers [79]. Previous work conducted on monkeys with focal ischemic lesions showed the importance of an early start of training. Sustained and repetitive exercises during the first 4 weeks after the onset of the lesions led to the prevention of loss followed by an expansion in the affected cortical territory [80]. The same results were noted in the case of the sensory cortex [81]. Moreover, various authors have also recorded a statistically significant link between the intensity of training and the improvement of daily activities [19, 82]. When the classical treatment is applied to stroke patients in a dedicated rehabilitation centre, most of the time the patient does not benefit from the therapy early enough and the time dedicated to each case is limited, thus resulting in a more inefficient therapy than that provided through virtual reality from home. Home-based VR therapy might offer an encouraging add-on or alternative solution early on after stroke, but also after discharge from the conventional therapy, prolonging required treatment and reinforcing clinical outcomes [83].

The use of VR for post-stroke rehabilitation also comes with several limitations. One example lies in the use of HMDs for immersive systems. Even though studies have pointed out the advantages of head-mounted devices in terms of depth perception and an enhanced sense of presence, both of which have been shown beneficial for the overall rehabilitation process and the possibility of a better translation of the achievements into the real world [84], they also come with downsides. Caution should be exercised when stroke survivors use the VR rehabilitation systems to avoid 'rehabilitation overdose'. The effects of the 'rehabilitation overdose' can impact the activity-rest balance and optimal cortical reorganization, demanding careful supervision by skilled professionals [85]. During immersive VR trials, some participants have reported several adverse effects such as dizziness and headache. There are also concerns around the acceptability of immersive VR by certain categories of patients, in particular older people, although older people are more likely to accept the non-immersive VR due to low cybersickness effects [83]. Extensive wearing of HMDs eventually results in neck discomfort and can influence the perception of distance [86]. Non-immersive virtual reality-based approaches may be more appropriate considering safety aspects (goggles-based immersive virtual reality makes the user unaware of the physical environment hazards) as well as the final goal of the intervention program (the reconnection with the reality around, with caregivers and family, better space-time orientation). Another important aspect regarding this choice is related to the sense of agency (feeling in control of one's actions) of our participants, most of them with neurocognitive disorders diagnosed after a stroke. This cognitive function is impaired in people post-stroke presenting sensorimotor deficits. Recent research suggests that this condition must be caused not only by a disturbed sensorimotor system and its impact on motor control, as post-stroke patients tend to misattribute actions executed also with the non-affected upper limb [87].

Ethical aspects regarding the use of VR in stroke rehabilitation

Moor's Law advanced technologies correlate with social and ethical impact [88]. VR-based approaches come with lots of questions regarding the appropriateness of using pioneering technologies in the treatment of frail and disabled people, mainly because it is not very well analysed in terms of long-term effects and generates unknown physiological, cognitive and behavioral potential changes [89]. This target population must benefit from cost-effective and safe interventions, integrated into clinical practice due not only to imposed regulations but first and more important, through clinical reasoning, respect, care and education [90]. Technology means not only hardware and software but also the intervention itself, which must be designed carefully, based on clinical evidence. The parameters of the functions trained are as important as the metaphors used in serious gaming. Technology has to be designed for and iteratively tested during its development by its target users. It has to integrate anticipatory ethics and developers need to have in mind its' foreseeable use, not only its' intended use. Special attention must be accorded to the aspects of personal data protection and the hacking possibility in such technologies, especially in the context of the Virtual Environment of Things, connecting the VR tools with the internet [91]. The way artificial intelligence is trained to develop users' interaction with technology needs also a careful approach and deep knowledge regarding the needs and limitations of the users. Another aspect is related to self-representation through avatars, especially in people with disabilities generated by central nervous system injuries [92]. Guidelines and regulations are emerging to direct VR development and use in all these regards [91].

An issue in VR systems is that patients report difficulty in transferring the acquisitions to everyday life [12, 93, 94]. This delay can prolong the duration of the rehabilitation period and its' individual and social costs. In comparison to the classical approach, VR also lacks the knowledge and experience of trained professionals, who are more flexible and can adapt more rapidly to the needs of every individual. Immersive VR rarely gives the therapist the possibility to see in real-time what the user experiences, thus making it impossible to adap the intervention in due time, if needed, to avoid physical injuries or psychological disturbances, traumatic stress disorder or even kinesiophobia. In frail populations, cognitive functions can be affected by VR, due to its ability to induce distortions in perception, exacerbating symptoms and disturbing reality orientation [95], even inducing feelings of insecurity. Physical and mental-health related risks may appear from VR motion-sickness, information overload, experience intensification bringing stress and frustration and difficulties to re-enter real environment after VR exposure [96]. Another aspect requiring attention is the necessity of acquiring new knowledge and learning new skills when using VR tools (avatars included), instead of easing the interaction between user and environment, which must be directed to meaningful real-life-like activities. Studies indicate that spatial information and ADLs -related skills can be transferred to real life after VR-based training [97]. The users must improve their life abilities to perform the activities of daily living in an optimized manner, training those functions required and improving their procedural memory, while the "extended cognition" inherent also to VR long-term exposure comes with neuroplasticity directed to other brain areas and networks than the ones in need [98]. The virtual environment and the actions the users have to perform during training activities must be designed accordingly to the real needs and weak points of the users.

Moreover, traditional physical therapy and complementary treatments, such as botulinum toxin are available in this instance, which can beneficially contribute towards a better recovery. It is also worth noting that most studies are short-term, with no follow-up results, therefore limiting the information about chronic patients [99]. Finally, the cost of immersive virtual reality technologies is still high and the proof of its benefits is limited, making it inaccessible to certain patients or not clinically worthwhile.

Conflict of interest

The authors declare that they have no conflict of interest.

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