Journal of Experimental and Clinical Medicine
https://dergipark.org.tr/omujecm

Review Article

J Exp Clin Med
2024; 41(2): 390-396
doi: 10.52142/omujecm.41.2.28

The effect of virtual reality based rehabilitation on cognitive functions in stroke patients: A review

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Received: 02.02.2024 • **Accepted/Published Online:** 03.04.2024 • **Final Version:** 19.05.2024

Abstract
Stroke stands as one of the primary global causes of disability and mortality. Post-stroke cognitive impairment (PSCI) emerges as a prevalent aftermath affecting over a third of the patients, with its incidence steadily rising annually. Notable clinical findings, that significantly affect participation in daily routines and life contentment, can be listed as; memory decline, concentration challenges, dependency in decision-making, and struggle in problem-solving. There is also a correlation among PSCI, dementia, and, disability rates. Therefore, cognitive rehabilitation strategies to improve cognitive functions are important components of stroke rehabilitation interventions. Traditional cognitive education, physical therapy, physical activity, psychotherapy, and complementary medicine practices are frequently used in the literature to rehabilitate PSCI. In addition to these advancements, the evolution of information technology has introduced alternative treatment approaches that can be utilized in Cognitive Rehabilitation (CR) applications such as Virtual Reality (VR). This review aims to assess the contribution of VR applications within CR specifically tailored for stroke patients.

Keywords: cognitive functions, cognitive training, neurology, stroke, virtual reality

1. Introduction

A stroke is a neurological disorder characterized by the sudden onset of symptoms and the rapid loss of focal and global cerebral functions without any apparent cause other than vascular factors. It ranks second among the causes of death worldwide. Stroke affects approximately 15 million people annually, and is stated as one of the primary contributors to long-term disability (1-3). It ranks third among the causes of disability in the world due to the physical and cognitive disabilities it creates (3). It is reputed that in 2019, there were approximately 101 million individuals who had a stroke all over the world. Such a numerical increase in the number of patients suffering from stroke causes stroke to be seen as a global problem (4). Post-stroke cognitive impairments (PSCI) typically emerge after three to six months and can be marked by noticeable cognitive dysfunction (5, 6).

In the literature, current studies have shown that medical advances in acute stroke treatment led to a decrease in mortality rates over the last 30 years (7). Despite the decrease in the mortality rates, the physical and cognitive disorders (CD) in the acute and chronic periods continue to increase for stroke survivors. In the study, in which eight countries participated and where the cognitive status of 3146 strokes (97%) and transient ischemic attack (3%) patients were analyzed, it was found that within two to six months after the stroke, 44% of the patients had general CD and 30-35% of stroke survivors continued to have impairments in a single cognitive domain (8). Recent meta-analysis studies revealed a PSCI prevalence of 53.4% within 1.5 years following a stroke. Among these cases, mild and major prevalence rates were reported at 36.4% - 38% and 16%, severally (9, 10). Studies have revealed that around 35.6% of stroke survivors encounter PSCI within the initial five years following the onset of stroke (11). Similarly, based on the findings of a meta-analysis, the prevalence of PSCI in the first year after stroke was shown to be 40%, and in a long-term follow-up study, it was emphasized that the prevalence of PSCI was 61% among individuals who survived 10 years after the stroke (10, 12). In addition to chronically

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experiencing cognitive problems, approximately two-thirds of stroke patients also have to struggle with cognitive problems in the acute phase (13). As can be understood from prevalence studies, CD is a serious problem that is most likely to be seen in stroke patients which is encountered both in the acute and chronic periods.

Cognition has several higher-level functions which can be sub-categorized into six neurocognitive domains (14). In the DSM-5 classification, these domains include language, learning and memory, social cognition, complex attention, executive function, and perceptual-motor function (15). CDs are often a major consequence of diseases such as Alzheimer's disease, vascular dementia, and stroke (16). Therefore, cognitive deficits may cause individuals to experience disruptions in their ability to carry out instructions for tasks, initiating self-directed activities, and problem-solving (17). Memory problems, attention deficit, and impairment in executive functions are among the most common PSCIs in stroke patients (18). Although the pathophysiology mechanism of PSCI is not fully understood, it is generally thought to occur as a result of lesions in important cognitive areas such as the hippocampus, white matter, and cerebral cortex (19). Damage may occur in only one of these areas, or more than one area may be damaged. PSCI clinically results in deficits in advanced brain functions including attention, memory, executive abilities, and visual/structural functions. These impairments significantly impact patients' daily activities and overall rehabilitation (20, 21). According to the current view in the literature, it is accepted that stroke has a more devastating effect on attention and executive functions compared to its effects on memory (22).

Stroke patients often experience clinical depression, marked by behavioral, cognitive, and emotional traits. Cognitive performance consistently intertwines with depressive symptoms, and early cognitive impairments in post-stroke individuals could foreshadow prolonged depressive tendencies (23). Furthermore, PSCI is linked to early and enduring limitations in activities and participation (24). Consequently, CDs leading to varying degrees of cognitive decline not only impact the life quality of individuals who have experienced a stroke but also pose significant challenges for their families and caregivers (25, 26). It is known that even though 50% of patients who are in positive physical condition experience cognitive problems and face limitations in reintegrating into normal life, current rehabilitation approaches focus more on the rehabilitation of motor deficits since it is considered that physical impairments have more debilitating aspects on patients than CD (19, 27). As there is a shortage of effective drug treatments given the absence of effective treatments for cognitive decline and dementia, investigating alternative strategies to alleviate PSCI should be regarded as a pressing public health concern.

The goal of Cognitive Rehabilitation (CR) is to enhance a person's capability to perceive, comprehend, and respond suitably to information, as well as to restore cognitive function through various methods, including the augmentation of neurotrophic growth factors. Additionally, CR endeavors to foster the development of acquiring additional abilities to compensate for cognitive limitations (25, 28). After a stroke, CR involves various types of cognitive training, including cognitive strategy training interventions, medication, physical therapy, and other approaches (29). Within the literature, two fundamental types of CR are identified in current clinical practice: restorative and compensatory rehabilitation. Restorative rehabilitation targets the restoration of lost functions through specific manual cognitive exercises, while compensatory rehabilitation focuses on enhancing the patient's utilization of aids and tools to overcome the disorder. CR techniques fall into two primary categories: traditional methods involving paper-and-pencil exercises and computer-assisted approaches. Both approaches utilize cognitive strategies to either rehabilitate or improve deficiencies in attention, concentration, visual processing, language, memory, reasoning, problem-solving, and executive functions (30). The common element of applied rehabilitation approaches is neural plasticity which is considered as the ability of the brain to adjust its response to changes in the environment or the lesions (31). Neuronal plasticity includes atrophic processes such as the deletion of inactive neurons or neuronal contacts and includes trophic processes such as neurogenesis and synaptogenesis (32). In this sense, the brain exhibits a remarkable capacity for remodeling through behavioral experiences triggered by diverse events and stimuli (33).

In recent years, the integration of Virtual Reality (VR) applications as a novel approach for rehabilitating motor, cognitive, and sensory deficits has shown promising outcomes (30, 34). VR consists of a range of information technologies that are designed to construct interactive environments by simulating real-world experiences where users are engaged. These activities increase motor learning and neuroplasticity by allowing the patient to practice fabricated activities through VR which they would not be able to perform or would struggle in physical reality. A study using magnetic resonance imaging found consistent results showing that the organization of the sensorimotor cortex increases motor learning and neuroplasticity (35). VR systems contain specialized software applications and input-output devices, replicating intricate and immersive experiences. By integrating telemedicine, robotics, and rehabilitation through computer-based methods (36, 37), VR opens a new era in rehabilitation, offering potential advantages to rehabilitation teams. VR facilitates the organization of activity difficulties based on a patient's real abilities and potential, granting the capability to regulate performance through visual and auditory feedback. In addition, these systems provide patients with the opportunity to suggest fun activities, increasing motivation and participation, strengthening commitment to rehabilitation, and allowing the creation of personalized rehabilitation programs.

Multiple studies validate the potential of VR in stimulating the reactivation and enhancement of diverse cortical functions, optimizing the effectiveness of the sensory cortex (37-39). Hence, VR stands as a therapeutic system within the literature, facilitating the rehabilitation of patients in particular areas such as attention, memory, language, executive functions, spatial cognition, perceptual abilities, and psychosomatic anxiety, employing sensory engagement via heightened visual and auditory feedback. This review aims to assess the impact of VR tools in CR for stroke patients.

2. Method

The study was identified by online searching of Scopus, PubMed, Web of Science, and Cochrane databases. The following search terms are used and combined; "virtual reality" or "virtual", "reality" or "virtual reality", "stroke rehabilitation" or "stroke", "rehabilitation" or "stroke rehabilitation", "cognitive rehabilitation" or "cognitive rehabilitation in stroke".

3. Virtual Reality and Its Types

VR is a technology that enables individuals to engage in a computer-generated simulation of an environment. Although the use of devices such as virtual reality headsets seems to have become widespread in the 1970s, there is a debate about the origin of such devices. Ivan Sutherland (1938), an American engineer, was one of the first researchers to explore the potential of computers for people to have experiences they could not have in real life. In 1960, cinematographer Morgan Heilig developed a single-user console called "Sensorama" that simulated all the senses in its user's environment. In Heilig's concept, the user could only view images passively, but many elements of his idea inspired Sutherland, who was a graduate student at Harvard at the time. In 1968, Sutherland invented the first computer-connected and head-mounted display system. This first virtual reality headset was named "The Sword of Damocles" due to its heavy weight and strange shape. VR applications have developed over the years and their use has accelerated in education, commerce, gaming, manufacturing, industry, and healthcare. Research has stated that virtual reality technology will have an important place among the important technologies and trends that will affect the field of healthcare by 2025 (40). As virtual reality technology becomes more accessible day by day and the cost of research and development activities decreases, interest in VR technology is increasing. Additionally, considering the positive results and the increase in research show that VR technologies will have an important place in the health sector in the future. Also, the importance given to health studies with VR applications and the number of studies will increase every passing day.

In the literature, VR applications are divided into five basic subheadings: immersive VR (full-immersive), augmented VR (semi-immersive), non-immersive VR (non-immersive), collaborative, and Augmented Reality. Full immersive VR is a costly type of VR that provides the user the impression that the virtual world and events they experience are real (41). For a holistic VR, a highly believable and intensely detailed virtual world, a powerful computer that can detect the user's movements and reactions and simultaneously adjust the environment according to these movements, and a piece of head-mounted display equipment connected to the computer that immerses the user in the virtual world are needed. Special equipment such as VR glasses, gloves, and sensors that detect body movements can be added for a high-quality VR experience (42). It is used in chronic pain management, stroke rehabilitation, cognitive rehabilitation of anxiety and post-traumatic stress disorder, and physical therapy protocols for spinal cord injuries. In non-immersive VR, is a non-interactive virtual experience. The virtual world can be navigated, and some activities can be performed, but the environment cannot interact directly with the user. Personal computers can be considered non-immersive VR when used for a realistic flight simulation or with a headset and joystick. Gaming devices such as PlayStation and Xbox are also examples of non-immersive virtual reality. It is used in physical therapy and rehabilitation to increase motor skills, attention and memory, and social skills in individuals with autism and through gamification. Semi-immersive virtual reality represents a blend of non-immersive and fully immersive VR. Users can explore a virtual environment using a computer screen or VR glasses, yet the experience lacks sensory input beyond visual data, limiting its immersive nature. Semi-immersive VR is the most widely used and most cost-effective type of VR after non-immersive. In collaborative reality, you are given the chance to meet and interact with people from different locations simultaneously in a virtual world. Augmented Reality is a technology that shows the user virtual additions to the real world through a screen. It places virtual elements into the real world. Glasses, smartphones, and tablets are used as the primary interface (43). It is used to increase joint range of motion in physical therapy, for prosthesis training, for balance training in vestibular diseases, and for visual-spatial training in traumatic brain injury.

VR provides users the opportunity to immerse themselves in environments that closely resemble real-life objects and experiences (e.g., home environment, sports training location, social environment). VR applications integrate computers, head-mounted displays, body tracking sensors, specialized interface devices, and real-time graphics to immerse patients within a computer-generated environment world that dynamically responds to head and body movements (44). This capability facilitates the enhancement of the patient's physical and cognitive capacities by creating scenarios and conditions that replicate an authentic three-dimensional environment. The unimpeded interface enables maximal interaction between the patient and the virtual world. Additionally, it enables the dynamic customization of VR training settings to accommodate individual participant needs and activity levels (45). Key factors in enhancing neural plasticity among patients with brain disorders in VR applications involve high-intensity, repetitive, and multisensory interactions within targeted tasks (46). Both commercial systems such as Nintendo Wii, and Xbox Kinect, among others, and customized VR services are utilized in clinics and research studies as part of the available options.

Positive results have been reported in the literature that VR applications in neurological rehabilitation improve motor functions in stroke patients. Studies have demonstrated that VR workouts lasting between 5 to 8 weeks, conducted 3 to 5 days a week for 45 minutes per day and totaling more than 15 hours, effectively enhance lower extremity motor function, balance, gait, and daily functionality. A systematic review, which combines randomized controlled trials (RCTs) assessing the impact of VR on upper extremity motor functions among stroke patients, revealed the effectiveness of VR in enhancing upper extremity function and daily activities in this patient group (47).

4. The Place of Virtual Reality Applications in the Treatment of Post-Stroke Cognitive Impairment

While VR applications appear promising in the neurorehabilitation of stroke patients according to literature, there is still a scarcity of studies demonstrating the efficacy of VR in CR. Debates persist regarding its effectiveness in PSCI. While certain controlled experiments suggest that VR facilitates cognitive enhancement compared to conventional treatment (46, 48), other studies suggest that VR doesn't significantly differ from conventional methods in improving cognitive functions (49). Zhang et al. (2021), in their study examining seven RCTs, emphasized that VR training did not have a significant benefit on CR. It has been pointed out that this may be because the main purpose of VR interventions is not to improve cognitive function and the lack of the applied procedure (49). Wiley et al. (2020), in the results of five studies evaluating the effectiveness of VR applications in CR in stroke patients, the conclusion drawn from the study indicated that VR treatment did not demonstrate superiority over traditional rehabilitation interventions (50). In addition to these views, Aminov et al. (2018), in four studies evaluating the results of VR-based rehabilitation on cognitive functions, discovered significant improvements through VR applications in enhancing cognitive functions (51). Xiao et al. (2022) also found in meta-analysis studies that VR applications showed more significant differences than traditional treatment under the Montreal Cognitive Assessment (MoCA) index (52).

Gau et al. (2021) found that although existing meta-analysis studies based on data from six high-quality RCTs showed superiority in general cognition, attention, and executive functions in groups using VR-based intervention in patients reporting mild cognitive impairment compared to control groups, semi-immersive treatment combined with classical rehabilitation It was emphasized that VR-based training created using the technique did not show a significant improvement in the general cognitive functions, motor functions and daily life activities of chronic stroke patients (23). The results of this study indicate a favorable impact of VR-based training on attention, executive function, and overall cognitive abilities in stroke patients. Zhu et al. (2021) similarly reported consistent positive outcomes in mild cognitive impairment or dementia patients in their systematic review (53).

In the study conducted by De Luca et al. (2018), it was observed that VR treatment demonstrated greater efficacy in enhancing attention, visuospatial challenges, and motor deficiencies compared to the control group receiving standard CR. At the same time, striking results show that the Nirvana (BTS Bioengineering Corp) VR device applied in the VR group provides more patient compliance with the treatment and allows patients to have longer training sessions, thanks to more motivating and entertaining virtual scenarios. Additionally, when both groups were compared at the end of the treatment, it was found that the experimental group was superior to the control group in many of the cognitive parameters, and this improvement was shown to continue in the experimental group even after a month (30). Faria et al. (2016) demonstrated significant improvements in cognitive functions in the VR group in their study in which they used a virtual city stimulation in which various daily activities were integrated with performance in VR applied to stroke patients. However, they achieved superior results in VR in general cognitive functioning, attention, and executive functions compared to the group receiving traditional treatment (54). In a follow-up study, the same authors compared the VR program with paper-and-pencil exercises and found greater improvements in overall cognitive functions in the VR group when their cognitive status was assessed with MoCA (55). In another study conducted on individuals with PSCI, both the experimental and control groups were included in a computer-based CR program, and the experimental group was additionally given VR training. As a result of this study, in which they demonstrated the superiority of VR in many parameters, the authors stated that adding computer-based CR training to VR training may have additional benefits (56). In another study, a puzzle game was developed using a VR base, and stroke patients with mild CD were included in the study. In addition to the routine rehabilitation program of both groups, the experimental group received a VR-based puzzle game, while the control group received traditional CR treatment. At the end of the study, while both groups showed improvement, no significant differences were found in baseline data in comparisons between groups. However, the experimental group showed greater improvements in executive function and visuospatial cognitive features compared to the control (57). In a current randomized controlled study, the effects of computer-assisted CR using a VR program developed based on self-efficacy were compared with the effects of traditional treatment. It has been shown that treatment using a VR program in hospitalized stroke patients has greater effects in terms of stroke self-efficacy, cognitive function, visual perception, daily living activities, and health-related quality of life compared to traditional treatment (58). Rose Sin Yi et al. (2024) examined twenty-five randomized controlled studies in which VR and CR treatments were applied in their systematic review and meta-analysis. While their studies found the superiority of VR applications over control treatments in improving global cognitive function, executive function, and memory, no superiority was shown in language, visual-spatial ability, and daily living activities (59). On the other hand, in a different systematic review and meta-analysis examining 150 studies, it was found that stroke rehabilitation with VR was effective in improving cognitive functions but was not superior to standard treatment (60).

Contemporary data substantiates the potential of VR training in aiding the rehabilitation of attentional processes among stroke patients. These processes augment VR's efficacy by fostering brain plasticity mechanisms through intricate pathways (61). These impacts could potentially link to the revival of various brain neurotransmitter pathways, such as the cholinergic and dopaminergic systems, during CR conducted via VR (62, 63). Different studies establish the relationship between cognitive and motor functions, emphasizing that especially carrying out training in a virtual environment can have positive effects on motor rehabilitation of advanced cognitive functions (62). It is also reported that the psychological well-being created by virtual environments will have positive effects on the patient's cognitive and motor results (64).

Some studies argue that the success of VR-based interventions cannot be solely attributed to increased dosage, frequency, or daily intensity (65-68), Gau et al.'s (2021) meta-analysis, through subgroup analysis, revealed that increased doses of VR treatment (exceeding 20 hours of intervention), higher frequencies (over four times a week), and greater daily durations (beyond 60 minutes a day) exhibited more positive impacts on cognitive abilities, motor skills, mood, and everyday activities improvement. Furthermore, it was suggested that VR training using head-mounted display devices (HMDD) may yield better behavioral outcomes in stroke patients (23). Contrary to this perspective, studies by Gamito et al. (2014) demonstrated no notable distinction between HMDD and semi-immersive VR induced by desktop screens in enhancing working memory and sustained attention among stroke patients (69). However, HMDD has some usage limitations such as being expensive, not easily transportable, and causing visual disturbances, which limits its widespread use in the literature.

5. Conclusion

Cognitive problems are frequently observed in individuals who have had a stroke, and current treatment searches in this field continue. Rehabilitation strategies to improve cognitive functions have an important place in stroke treatment. One of these treatment methods is the use of VR. Cost-effective, portable, easy-to-use VR-based applications seem to be usable in the cognitive rehabilitation of chronic stroke patients with post-stroke CD. According to the literature review results, the striking point is that VR applications are needed to simultaneously support the motor and cognitive functions of patients who suffer from both physical and cognitive function loss. Therefore, forthcoming research requires more extensive double-blind, randomized controlled studies featuring larger sample sizes to address uncertainties and inconsistencies concerning the long-term effects of VR applications on cognitive functions among stroke patients.

Conflict of interest
All authors declared no conflict of interest.

Funding
None to declare.

Acknowledgments
None to declare.

Authors' contributions
Concept: S.G.Ö., M.K.A., A.K.K., Design: S.G.Ö., M.K.A., S.A., Data Collection or Processing: S.G.Ö., H.E.A., M.O.K., Analysis or Interpretation: A.K.K., H.B.G., M.O.K., Literature Search: A.K.K., S.A., H.B.G., Writing: M.K.A, A.K.K., H.E.A.

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