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Effect of Virtual Reality on Neural Recovery in Patients with Stroke: A Systematic Review

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Abstract

Background: Stroke is a vascular injury of the brain that leads to neurological deficits and significant disabilities. Mirroring interventions such as virtual reality (VR) have proven to be effective in several studies. However, no study has systematically reviewed their effects on neural recovery in stroke patients.

Objectives: To systematically review research on the effects of virtual reality (VR) on neural recovery in post-stroke patients to find the best evidence.

Methods: Four electronic databases; Web of Science, PubMed, Scopus, and PEDro; were searched for articles published between 2011 and 2022. This trial included English randomized controlled trials that compared VR with other comparators in patients with stroke. The PEDro scale was used to assess the quality of the eligible studies.

Results: Eight studies with 220 participants were included. All the studies were good to excellent on the PEDro scale. Virtual reality had strong evidence for improving neural recovery in patients with stroke.

Conclusion: Virtual reality should be added to the traditional rehabilitation program for patients with stroke to improve neural recovery in patients with stroke. Improved neural recovery may be a mechanism beyond improved motor recovery after rehabilitation with VR.

Key Words: *Mirror Neurons, Neural recovery, Stroke, Systematic review, Virtual reality.*

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Introduction

Stroke is a neurological condition caused by vascular injury to the central nervous system (CNS), infarction, and hemorrhage. It leads to hemiparesis or hemiplegia and hence disability (1-3).

Physical therapy can induce adaptive plasticity in the structure and function of the undamaged brain toward recovery. However, it is not an easy task; it is usually

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limited and challenged by the poor volitional capacity of patients (1). An interesting solution to this challenge is to target mirror neurons via mirroring interventions such as virtual reality. These interventions code and represent tasks in the motor cortex providing an easy way to reach the motor system and improve function (4).

Virtual reality (VR) is a mirroring intervention in which motions of the less affected side are filmed with a camcorder and the patient sees its image projected on the monitor over their hemiplegic limb (5). It has several advantages over other traditional treatments; it is cheap, portable, easy, and provides patient motivation and feedback (6).

Virtual reality improves several outcomes related to motor rather than neural recovery in stroke patients (5,7,8). So**, Viñas-Diz & Sobrido-Prieto (2016)** called researchers to study changes in cortical reorganization as a mechanism for improving the mentioned outcomes. Several authors responded and conducted studies in this area **(**10-16) and found positive results. **Hao et al**. **(2022)** studied the mechanisms of neural plasticity and its relationship to function in a systematic review. They found several neurophysiological changes such as improved interhemispheric balance, cortical connectivity; mapping, and activation. However, the previous review was limited by not including neural plasticity as the primary outcome and by including many case studies and poor-quality studies. Therefore, this study aimed to systematically review the research on the effects of VR on neural recovery in post-stroke patients to find the best evidence.

Subjects and Methods

The present systematic review was conducted by searching four electronic databases; Physiotherapy Evidence Database [PEDro], PubMed, Web of Science [WOS], and Scopus, from 2011 to 2022. In addition, a manual search was carried out. The aim was to determine the best available evidence about the effects of VR on neural recovery in post-stroke patients. The research ethics committee-faculty of Physical Therapy approved this study (No: P.T.REC/012/003562).

Eligibility criteria:

The criteria for inclusion of the studies were presented in **Table (1)**. Trials with designs other than randomized trials, those that assessed combined interventions, and/or published in non-English languages were excluded.

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Table (1): Inclusion criteria; participants, interventions, comparator, outcomes, and study design (PICOS).

PICOS	
Participants (P)	Post-stroke patients aged >18 years.
Interventions (I)	Virtual reality reflection therapy
Comparator (C)	Any comparator (as standard care or placebo).
Outcome (O)	Neural recovery.
Study design (S)	Published full text of English randomized trials.

Search strategy:

Electronic databases *(*PubMed, Scopus, WOS, PEDro) were searched from 2011 to 2022 using keywords; Stroke, cerebrovascular accident, hemiplegia, traumatic brain injuries, acute or vascular accident, brain, and neural activity.

Study selection:

Two reviewers (AMH & AAI) independently checked the studies identified by all databases for criteria of eligibility via titles and abstracts. They excluded any study that violated the criteria of inclusion. Then, the eligible/inclusive studies were downloaded as full texts and assessed for eligibility.

Data extraction:

Details of all the included studies such as the age, size, and gender of the patients, treatment (type, dose, frequency), outcomes, and findings A data collection form was used to extract and record the key features of each trial including the. The same two reviewers, who were selected, extracted these data from the included studies.

Quality assessment of the included studies:

The physical therapy evidence database scale (PEDro) was used to evaluate the quality of the included studies. Discussion between the two independent reviewers was done to reach an agreement and if needed a third reviewer (GMN) was included. Studies that achieved a score ≥ 9 points are rated excellent, studies that achieved a score of 6-8 are rated good, studies that achieved scores 4-5 are rated average, and studies that achieved ≤3 are rated poor (18).

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Results

Four hundred thirty-one (431) studies were identified from all electronic and manual searches. After duplicate studies were excluded, a total of 315 trials were screened, and 282 trials were excluded by title & abstract. Thirty-three studies that appeared to follow the criteria of inclusion were searched for their full text, of which 8 were included and met the inclusion criteria of this review which addressed virtual reality and neural recovery in stroke (**Figure 1**).

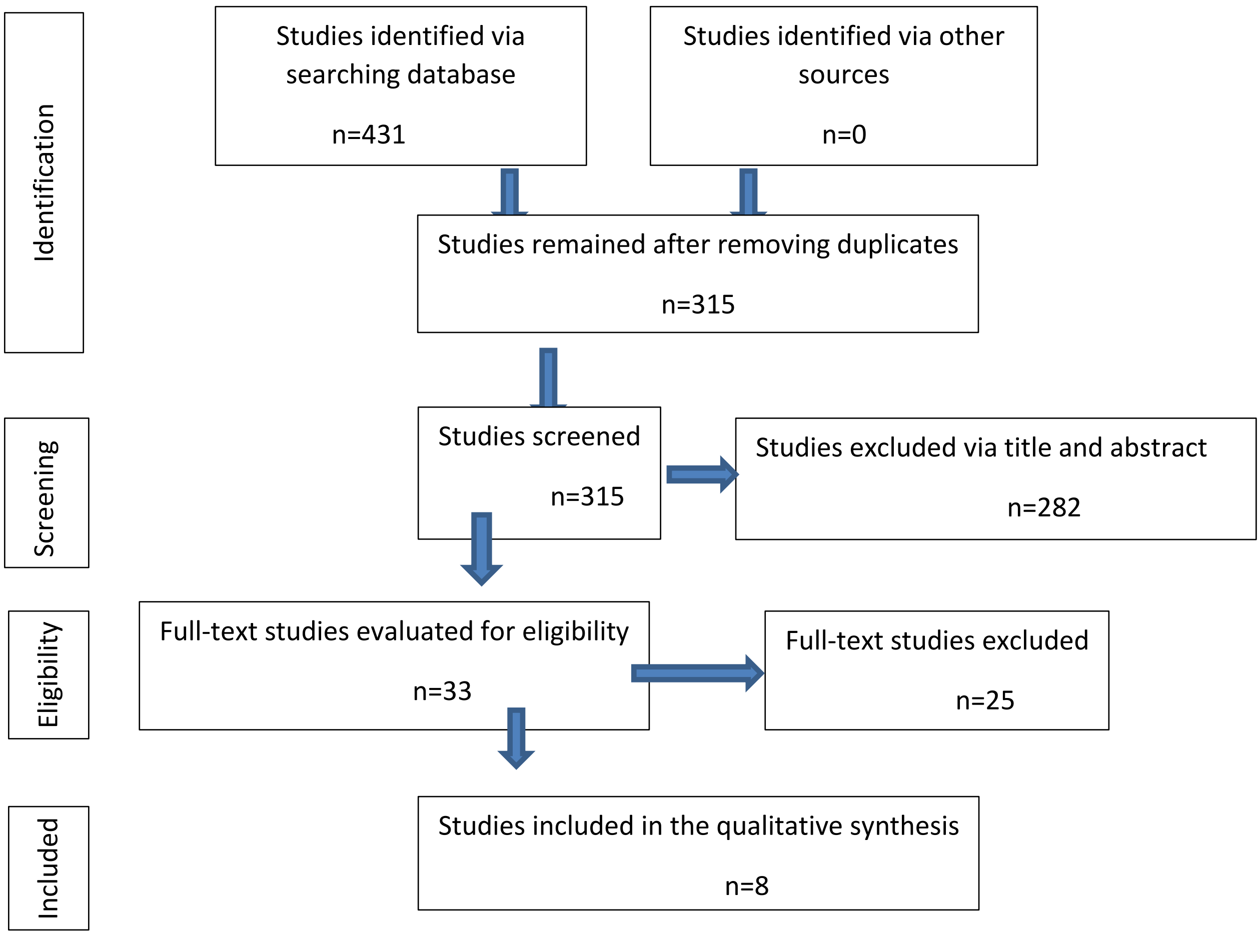

Fig. (1): PRISMA flow chart.

Characteristics of the included studies:

This review included eight studies and their characteristics regarding participants, interventions, outcomes, comparators, and results was presented in **Table (2)**.

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Table (2): Studies Characteristics

Study	Diagnosis/ stage	Experimental		Control		Conclusion
		Participant	Intervention	Participant	Intervention	
1. Calabrò et al. (11)	Ischemic supra-tentorial stroke	N= 12 (7M) 60 (± 4) y	Robotic-assisted gait training (RAGT)+ VR 5 sessions (45 min)/W/8W	N= 12 (7 M) 63 (± 6)y	RAGT	VR + RAGT induce higher cortical activations
2. Ballester et al. (10)	Chronic stroke	N= 17 (8M) 65.05 (± 10.33)y	Home-based UL rehabilitation using VR (Hit, Grasp, and Place). 5 sessions (20 min)/W/3W	N= 18 (6M) 61.75 (12.94)y	20 min OT task at home (stacking and unstacking of plastic cups with RT and LT hand).	VR enhanced the organization of corticospinal pathways.
3. L. Chen et al . (16)	Subacute stroke	N= 18 (10 M) 57.8 (± 8.4) y	VR training of reaching and reach to grasp 5 sessions (45 min)/W/2W.	N= 18 (10M) 58.4 (± 9.3) y	45 min OT (grip strength, selective finger movement, and ADLs)	VR decreased the amplitude of CNV in the cortical areas more than in the control.
4. Huang et al. (15)	Stroke> 3 months	N= 15 (6M) 50.80 (±12.32)y	VR training (VRT), 6-10 tasks were assigned in each session. 16 sessions (60 min/ 2 to 3 /week.	N=15 (4M) 58.33 (±11.22)y	OT (climbing ladder, peg board & stacking cones with UL).	BDNF decreased slightly in the OT group but was significantly higher in the VR group.
5. Mekbib et al. (12)	Stroke<3 months	N= 12 (9M) 52.17 (± 13.26) y	VR + OT (reaching, grasping, and releasing) 4 sessions (1-h VR plus 1-h OT)/W/ 2 W.	N= 11 (8 M) 61.00 (± 7.69) y	OT (ADLs, balance, gait training, weight shift, and UL functional movements)	VR improved the functional reorganization of the motor system.
6. Shin & Lee (14)	3 months >Stroke> 3 weeks	N= 20 (10 M) 57 (± 12.8) y	Game-based VR hand motor training with RAPAEL®	N= 16 (7 M) 63.7 (± 8.6) y	Conventional OT alone	OxyHb increased significantly in the right

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			5 sessions (1h)/W/4W			affected SMC VR only.
7. Song et al. (13)	Stroke > 6 months	N= 5 (3 M) 64.20 (± 7.08) y	VR-based bilateral arm training (ADLs, a visual perception and cognitive rehabilitation, store). 5 sessions (30 min VR+1h OT)/W/4W.	N= 5 (3 M) 60 (± 10.88) y	Bilateral arm training (switching on lights & arranging chest of drawers & kitchen)	Both groups improved in brain activity.
8. Wang et al. (19)	The subacute phase of stroke (1-6 months)	N= 13 (11 M) 55.33 (± 8.40) y	Leap Motion-based VR and OT 5 sessions (45min)/W/4W .	N= 13 (11 M) 53.38 (± 7.65) y	Conventional OT alone	VR increased the activation intensity of the contralateral SMC (neural reorganization more than the control.

y: year; VR: virtual reality; OT: occupational therapy; ADLs: activities of daily living; N: number: M: male; F: female: H: hour; W: week; RAGT: robotic-assisted gait training; CNV: contingent negative variation.

***Participants**:*

This review included 220 participants in total (ranging from 10 to 36, for individual studies) with a mean age was from 51-65 years and illness duration from 1 to >6 months. Fifty-six percent of the participants were male. **Table (2)** includes the participants' characteristics in each study.

***Interventions**:*

Interventions addressed in the included studies of this review were VR alone (10; 13-16) or added to RAGT (11) or OT (12; 15). Interventions were done as 2-5 sessions weekly, lasting from 20 to 90 minutes for 2-8 weeks. **Table (2)** presented the interventions addressed in studies of this review.

***Outcomes**:*

The primary outcome of the current study is neural recovery. For a measure of the neural recovery/ cortical activation, three studies (11,13,16) used EEG, 1 study (10) used Navigated Brain Stimulation (NBS), 1 study (15) used Serum sampling for molecular biomarkers including BDNF, 2 studies (12,19) used fMRI, and 1 study (14) used NIRSscout® system for changes of oxygenated hemoglobin (OxyHb) (**Table 2**).

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Quality assessment:

There was no to low risk of bias in the included studies of this review as identified by having a score ≥7 (good to excellent quality) on the PEDro scale. See **Table (3)** for more details.

Table (3): PEDro scale

Article	1	2	3	4	5	6	7	8	9	10	11	Total	Classification
1. Calabrò et al. (11)	Yes	1	1	1	1	1	1	1	0	1	1	9/10	Excellent
2.Ballester et al. (10)	Yes	1	1	1	1	0	0	1	0	1	1	7/10	Good
3. L. Chen et al. (16)	Yes	1	1	1	1	0	1	1	0	1	1	8/10	Good
4. Huang et al. (15)	Yes	1	1	1	1	0	1	1	0	1	1	8/10	Good
5.Mekbib et al. (12)	Yes	1	1	1	1	0	1	1	0	1	1	8/10	Good
6. Shin & Lee (14)	Yes	1	1	1	1	0	0	1	0	1	1	7/10	Good
7. Song et al. (13)	Yes	1	1	1	1	0	0	1	0	1	1	7/10	Good
8. Wang et al. (19)	Yes	1	1	1	1	0	1	1	0	1	1	8/10	Good

Effect of VR on neural recovery of stroke:

This study documented strong evidence for the positive effect of VR on neural recovery post-stroke as seven studies, out of eight, with good to excellent quality reported significant improvement in neural recovery; cortical organization (10,12), cortical activation (11,16), serum biomarkers (15), and OxyHb (14) after VR alone or combined with other interventions (RAGT [11] or OT [12; 15]) compared with control group (RAGT or OT). Only one study with good quality (13) found that VR is similar to OT in improving neural recovery (brain activity). So, VR alone or combined with other interventions had good to excellent evidence in improving neural recovery in patients post-stroke. **Table (2)** presents the conclusions of the studies of this review.

Discussion

This review investigated the best evidence about the effect of virtual reality on neural recovery in patients post-stroke. It included eight RCTs with 220 patients in total. All trials had good to excellent quality (the PEDro scale median score was 7.75 points, denoting a high quality). Seven studies reported improved neural recovery (cortical reorganization and activation, and serum biomarkers) after VR alone or added to RAGT or OT, compared to a control intervention (RAGT or OT). One study reported that VR did not improve neural recovery more than control. So, there is strong evidence for the effects of VR on neural recovery in patients post-stroke.

Recent methods of rehabilitative interventions for stroke patients (e.g. VR) lead to neuroplasticity (reorganization) of the brain more than traditional ones, which is responsible for motor or functional recovery (20-22).

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One previous systematic review (18) studied the effects of mirroring interventions including VR on motor recovery. It found only one study (5) which reported a significant enhancement in the VR compared to the control on walking, function, and balance, in 25 patients post-stroke. It did not identify any study that addressed neural recovery as an outcome. The present review found that VR improves neural recovery in post-stroke patients. This may explain the mechanism behind the improvement of the clinical outcomes included in the study of **In et al. (5).**

In another systematic review, **Hao et al. (17)** reported that VR can improve clinical outcomes such as motor function via several neurophysiological changes such as improved interhemispheric balance, cortical connectivity; mapping, and activation. This review came in line with our review. However, the previous review is limited by not including neural plasticity as a primary outcome and by including many case studies and poor-quality studies. Most of the included studies had quality less than good.

This review had some limitations in the trials that were included. All of the trials that were included but one had no blinding of the therapists and all studies had a small sample size. As well, the external validity or applicability of results to a wider population is reduced. Interventions were variable in the dosage; two to five sessions weekly lasted from 20 to 90 minutes for two to eight weeks. Fifty percent of the included studies included additional treatments which increased the duration of treatment in the experimental or VR group, so we cannot guarantee that the improvements were from VR intervention. The coming studies should be homogenous in dosage and should include VR alone in the experimental group.

Conclusions

In light of this review, strong evidence for the efficacy of VR, alone or combined with other interventions, in improving the neural recovery of patients post-stroke was documented.

Declaration of Conflicts of Interest

The authors disclose that there are no personal or financial conflicts.

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