

Effects of Virtual Reality-Based Mirror Therapy on Upper Extremity Motor Function, Manual Performance and Gross Manual Dexterity Among Stroke Patients: A Meta-Analysis

FOUZIA HUSSAIN†, MAHNOOR KHURSHEED†, SUMERA AFZAL†, MUHAMMAD USMAN KHAN‡, AHAD HASAN‡, and SYED MEERAN HASNAIN‡

Ziauddin College of Physical Therapy, Ziauddin University, Karachi, PAKISTAN

†Denotes graduate student author, ‡Denotes professional author

ABSTRACT

International Journal of Exercise Science 17(7): 1219-1234, 2024. In recent years, innovative technologies have gained prominence in stroke patient rehabilitation worldwide, with virtual reality-based mirror therapy (VRBMT) emerging as a notable example. Hence, the present study aims to determine the efficacy of VRBMT on upper extremity motor function, manual performance, and gross manual dexterity among stroke patients. The systematic search utilized Population, Intervention, Comparison, Outcome, and Design (PICOD) paradigm, and the study searched was based on 2012-2023, utilizing different databases. The meta-analysis data was evaluated using MedCalc version 18.11.3. The Pooled effect size mean was statistically examined using a fixed and random effect model. Among the 6 studies selected, 4 studies involving upper-limb stroke patients were identified between the VRBMT. Pooled analysis of VRBMT revealed no significant effect on motor function [standardized mean difference (SMD) 0.815 ; 95% CI 0.00 to 81.37; P = 0.5562]. The remaining 2 of 6 studies participated in the study of the manual performance stroke patients (SMD 0.869; 95% CI 0.00 to 93.22; $P = 0.0684$). The pooled analysis of VRBMT revealed no significant effect. The last 2 of 6 included studies on gross manual dexterity in stroke. The pooled analysis also showed no significant effects on VRBMT (SMD 0.198; 95% CI 0.00 to 0.00; P = 0.6951). The present study concluded although VRBMT exhibits potential as a novel method for stroke rehabilitation, its effects on gross manual dexterity, manual performance, and upper extremity motor function are not statistically significant may be due to a limited number of studies on VRBMT in stroke patients.

KEY WORDS: Exergaming, mirror movement therapy, physical therapy, stroke, virtual reality

INTRODUCTION

In 2020, the World Stroke Organization published that stroke was the second-highest cause of mortality globally and the third highest accounting for mortality and disability combined (17). A report suggested that in 2010, a total of 33 million cases of stroke had occurred worldwide (26). The Burden of Disease from 1990 to 2019, greatly increased, the incidence of stroke increased by 70% and stroke's death by 43% (17). The majority of stroke deaths occurred in lower and middle-income countries, accounting for 86.0% of stroke-related deaths and 89.0% of the associated Disability-Adjusted Life Years (2).

In the meantime, the incidence of stroke significantly decreased by 42% in high-income countries. As per the findings of the Global Burden of Disease, the occurrence of stroke has seen a decline; various factors such as the age distribution, gender, and geographical location of affected individuals contribute to an increase in the socioeconomic burden associated with stroke over time. According to reports, the incidence of stroke is highest in China, impacting an estimated 331–378 people per 100,000 life years. Latin America reported the lowest incidence, at 85–100 per 100,000 life years, but Eastern Europe follows closely at 181-218 per 100,000 life years (19).

Pakistan is the sixth most populous country globally and a study conducted in Karachi showed that a stroke prevalence of 4.8% and 19.1% highest in the region and the estimated yearly incidence of stroke is 250/100,000 in Pakistan (7,14,16). A large-scale, population-based approach is needed to study the prevalence of stroke in rural and urban areas of Pakistan (27). According to Hashmi et al., 2013 Stroke rates among middle-aged individuals are significantly elevated in Pakistan, Russia, India, Brazil, and China (9).

A stroke is characterized as an acute neurological deficit localized to a specific area, resulting from vascular damage (such as infarction or hemorrhage) within the central nervous system. Symptoms of stroke include unilateral limb weakness, headache, nausea, and vomiting are the most common clinical features of stroke (31). Many post-stroke patients suffer from impaired upper extremity motor function, which is highly related to limitations in daily living and a poorer quality of life. Motor impairment of the upper extremity has been reported in about 80% of acute strokes, reduced manual performance in approximately one-half of individuals after stroke, and losses in manual dexterity sustained to the chronic phase (30). Therefore, it is highly related to the ability to perform manual tasks and activities of daily living hence an important target for rehabilitation after stroke (5). Impaired Gross manual dexterity is a significant contributor to functional disability after stroke (25).

Stroke is a major health issue, and even more frustrating is that the few effective treatments are limited by thrombolytic therapy that can only be facilitated through recombinant tissue plasminogen activator, which needs to be administered within three hours of stroke onset. Rehabilitation presents an individual who has suffered a stroke with the optimal chance for maximal recovery (19). There are a variety of physiotherapy treatment options for stroke patients. Range of motion, functional electrical stimulation strength training and Virtual Reality (VR) are just a few of them (29).

Virtual Reality-based Mirror treatment (VRBMT) is a new approach in the treatment of stroke patients (22). Mirror therapy (MT) is a method of changing the structure and function of the brain. Viral replication systems can induce plasticity in neurons and are an effective way of modifying how functionality recovers after a stroke. Abiding by the principle of VRBMT is also a promising, effective, and advanced method of treatment compared to traditional MT. The first one was how VRBMT can cause plasticity and reorganization of the brain's neuron patterns to create conditions where it is feasible to develop this new technique, especially for the effect of stroke on an adult's brain (1). The present review article is aimed at investigating the influence

of Virtual Reality-Based Mirror Therapy on individual outcomes regarding upper limb motor function, individual manual functioning, and gross manual dexterity in stroke patients.

METHODS

Protocol registration

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) criteria were followed in the execution of the current meta-analysis. The study's characteristics and procedure were registered under the CRD42024540772 registration number in the international PROSPERO database for systematic reviews and meta-analyses. This research was carried out by the ethical standards of the International Journal of Exercise Science (24).

Search strategy

Two independent reviewers conducted a comprehensive search for studies published between 2012 and 2023 on PubMed, PEDro, CENTRAL, MEDLINE, and CINAHL from January 2024 to April 2024. We looked through Open Gray for unpublished, relevant articles. The titles and abstracts were searched using Boolean operators (AND, OR, and NOT) combined with Medical Subject headings (MeSH) and keywords; "Virtual Reality" OR "Mirror therapy" AND ("Stroke") AND ("motor function") AND ("Upper limb function) AND "manual performance" AND "gross manual dexterity". Citation search was used to locate studies that were cited by authors in bibliographies or by chosen publications. Articles with potential relevance were filtered using the PICOD framework and inclusion and exclusion criteria.

Priori review

The selection criteria were considered and the efficacy of VRBMT was changed to include its comparison with other interventions, and all outcome measures of motor function, manual performance, and gross manual dexterity were included in the meta-analysis.

Inclusion and exclusion criteria

The PICOD approach stands for Population, Intervention, Comparison, Outcome, and Design was used to select the studies.

Population: Stroke patients. Intervention: VRBMT. Comparison: Mirror therapy, standard treatment, and occupational therapy. Outcome: Fugl-Meyer Assessment (FMA), Manual Function Test (MFT), and Box and Block Test (BBT). Design: Only Randomized Controlled Trials (RCTs) were included in the study.

Data extraction and quality assessment

All data were obtained as provided by the included studies following CRD and Cochrane's advice. The provided information for the included RCTs was divided into demographics, such as age, stroke period, study design, VRBMT amount and frequency, as well as the outcome measures, including upper extremity motor function, manual performance, and gross manual dexterity, with the FMA, MFT, and BBT scales used, respectively. For quality assessment, independent performance by two reviewers followed by a discussion was aimed at eliminating potential bias and enhancing the review's quality because it corresponds to the methodology, evaluates the study's internal and external validity, guarantees that the findings are applicable for practice, and represents a frequently used method in high-quality sources. Types of risks assessed for quality measurement including selection bias – randomization, and allocation concealment; performance bias – blinding, and detection; attrition bias – incomplete outcome data; and reporting bias – selective reporting of outcome are listed.

Data Analysis

The statistics software MedCalc 18.11.3 determined the results of a meta-analysis. The main aim of this review is to find upper extremity motor function, manual performance, and gross manual dexterity as a result measure. Both VRBMT and control groups presented RCTs with baseline, and post-treatment data were included. Fixed effects and random effects models were used to assess the pooled effect size estimations, while the mean, standard deviation, and 95 percent confidence intervals for the Upper extremity motor function, manual performance, and gross manual dexterity score were applied to the experimental and control group then the statistical software was utilized. Moreover, the heterogeneity in the model was measured by calculating I2; the values indicated: no heterogeneity (0%-40%), moderate heterogeneity (30%-60%), substantial heterogeneity (50%-90%), and considerable heterogeneity (75%-100%). Furthermore, the fixed model will be calculated with mild to moderate heterogeneity, and the random-effect model will calculate with considerable, high heterogeneity. In addition, the effect sizes for all analyses small 0.2-0.49, moderate,.50 to.79, large,.80 or above were applied to, with p<0.05 was considered statistically significant.

RESULTS

Study Identification

A search of citations and electronic databases identified a total of 182 studies. Six RCTs published between 2012 and 2023 that met the selection criteria were included in this evaluation. (Figure 1).

Table 1 provides a comprehensive review of the trials as well as participant characteristics on upper extremity motor function, manual performance, and gross manual dexterity among stroke patients.

Efficacy of Virtual Reality-based Mirror Therapy

Motor function: Four out of 6 included studies measured motor function in upper-limb stroke patients (Table 2 and Figure 2). All 4 studies measured motor function by FMA-UE (12,21,22,28). A fixed effects model was chosen and there was no significant heterogeneity (I2=0.00%). Pooled analysis showed no significant effects of VRBMT (SMD 0.815; 95% CI 0.00 to 81.37; P = 0.5562). (Table 2 and Figure 2).

Figure 1: PRISMA Flowchart for Study Selection.

	Author					Intervention			Conclusion
S. No.	name with the year	Stages of Stroke	Mean age	Design	Types of VR	Experimental group	Control group	Outcome Tools	
$\mathbf{1}$	In, et al., 2012(12)	Chronic stroke	63.45 to 64.50 years	RCT	NIVR using reflection therapy	$n=11$ Received VR and MT for thirty minutes each day, five days a week, for a total of four weeks	$n=8$ Use home for a treatment total of four weeks, five days a week, for thirty minutes each	FMA-UE, MFT, BBT	VR with MT and home-based exercises are effective for upper extremity motor function, manual performance, and manual gross dexterity in stroke patients
$\overline{2}$	Choi, et 2019 al., (3)	Chronic stroke	58 to 59.58 years	RCT	IVR using gesture recognition mirror	$n=12$ Received traditional, MT, and VR therapy 5 30 weeks of day, minutes \mathbf{a} three days a week	$n=12$ Received traditional therapy 5 weeks of 30 minutes a day, three days a week	MFT	Combine MT and VR therapy was found be to effective the in of improvement manual performance in stroke patients
3	2021 Lin, (21)	Chronic Stroke	49 to 58 years	RCT	IVR by usage of scenario the VRBMT system	$n=9$ nine weeks, For VRBMT for got fifty minutes a day, two days a week	$n=9$ Received MT for 50 minutes every day, twice a week, for nine weeks.	FMA-UE	VRBMT was found to be effective in the improvement of manual performance in stroke patients
$\overline{4}$	Mekbib, 2021 (22)	Chronic stroke	52 to 61 years	RCT	IVR by using a VR system to stimulate and activating MNs	$n = 12$ Received VRBMT receive VR to intervention (8 h within 2 weeks)	$n = 11$ Received Occupational therapy for 8-h with 2 weeks	FMA-UE	VRBMT was found to be more effective in improvement of extremity upper motor function as compared to occupational therapy in stroke patients

Table 1. Summary of the studies on upper extremity motor function, manual performance, and gross manual dexterity.

International Journal of Exercise Science http://www.intjexersci.com

Int J Exerc Sci 17(7): 1219-1234, 2024

NIVR: Non-Immersive Virtual Reality; MT: Mirror therapy; FMA-UE: Fugl-Meyer Assessment Upper extremity, MFT: Manual Function Test; IVR: Immersive Virtual Reality; VRBMT: Virtual Reality-Based Mirror Therapy; MNs: Mirror neurons; BBT: Box and Block Test

Study	N1	N ₂	Total	SMD	$\ensuremath{\mathsf{SE}}$	95% CI	T	$\mathbf P$	Weight (%)			
									Fixed	Random		
In, et al., 2012	11	8	19	0.937	0.469	-0.0528 to 1.927			23.15	23.15		
Lin, et al., 2021	9	9	18	0.877	-0.124 0.472 to 1.878				22.86	22.86		
Mekbib, al., et 2021	12	11	23	1.168	0.258 to 0.438 2.079				26.6	26.6		
Sip, et al., 2023	10	10	20	0.316	-0.590 0.431 to 1.221				27.40	27.4		
(fixed) Total effects)	42	38	80	0.815	0.226	0.365 to 1.264	$\overline{4}$	θ	100	100		
Total (random effects)	42	38	80	0.815	0.226	0.365 to 1.264	$\overline{4}$	θ	100	100		
Heterogeneity test												
Q	2.0789											
DF	3											
Significance level	$P = 0.5562$											
I ² (inconsistency)	0.00%											
95% CI for I ²	0.00 to 81.37											

Table 2. Effects of Virtual Reality-based Mirror Therapy using FMA-UE.

Figure 2. Forest plot effects of Virtual Reality Mirror Therapy on Upper extremity motor function.

Manual Performance

Two out of 6 included studies measured the manual performance of stroke patients (Table 3 and Figure 3). All the 2 studies measured manual performance by MFT (12,3). A random effects

International Journal of Exercise Science http://www.intjexersci.com

model was chosen and there was moderate heterogeneity $(I^2=69.89\%)$. Pooled analysis showed no significant effects of VRBMT (SMD 0.869; 95% CI 0.00 to 93.22 ; P = 0.0684). (Table 3 and Figure 3).

Study	N1	N ₂	Total	SMD	SE	95% CI	T	$\mathbf P$	Weight (%)		
									Fixed	Random	
In, et al., 2012	11	8	19	0.294	0.446	-0.648 to 1.236			49.94	49.98	
Choi, et al., 2019	12	12	24	1.444	0.446	0.519 to 2.369			50.06	50.02	
Total (fixed effects)	23	20	43	0.87	0.315	0.233 to 1.507	2.757	0.009	100	100	
Total (random effects)	23	20	43	0.869	0.575	-0.292 to 2.030	1.512	0.138	100	100	
Heterogeneity test											
Q	3.3207										
DF	$\mathbf{1}$										
Significance level	$P = 0.0684$										
I ² (inconsistency)	69.89%										
95% CI for I ²	0.00 to 93.22										

Table 3. Effects of Virtual Reality-based Mirror Therapy on manual performance using MFT

Figure 3. Forest plot effects of Virtual Reality Mirror Therapy on manual performance

Gross Manual Dexterity

Two out of 6 included studies measured gross manual dexterity in stroke patients (Table 4 and Figure 4). All the 2 studies measured gross manual dexterity by BBT (12,11). A fixed effects

model was chosen and there was no heterogeneity $(I^{2}=0.00\%)$. Pooled analysis showed no significant effects of VRBMT (SMD 0.198; 95% CI 0.00 to 0.00; P = 0.6951). (Table 3 and Figure 3).

Study	N1	N ₂	Total	SMD	SE	95% CI	T	${\bf P}$	Weight (%)			
									Fixed	Random		
In, et al., 2012	11	8	19	0.0587	0.444	-0.878			35.88	35.88		
						to 0.995						
Hsu, et al., 2022	18	17	35	0.276	0.332	-0.400			64.12	64.12		
						to 0.952						
Total (fixed	29	25	54	0.198	0.266	-0.336	0.745	0.46	100	100		
effects)						to 0.732						
Total (random	29	25	54	0.198	0.266	-0.336	0.745	0.46	100	100		
effects)						to 0.732						
	Heterogeneity test											
Q	0.1536											
DF	1											
Significance level	$P = 0.6951$											
I ² (inconsistency)	0.00%											
95% CI for I ²	$0.00 \text{ to } 0.00$											

Table 4. Forest plot effects of Virtual Reality Mirror Therapy on Gross Manual Dexterity using Box and Block test

Figure 4. Forest plot efficacy of Virtual Reality Mirror Therapy on Gross Manual Dexterity

Risk of Bias of Assessment

Cochrane risk of bias of assessment is presented in Table 5.

DISCUSSION

VR is becoming an important tool in the therapy and management of motor dysfunction (13, 23). In this review, we examined the impact of VRBMT on the following domains: upper extremity motor function, manual performance, and gross manual dexterity in patients with stroke. This study systematically reviewed the RCTs in an attempt to clarify the virtual effects of VRBMT on therapy. The outcomes of this meta-analysis revealed that VRBMT did not significantly enhance stroke patients' gross manual dexterity, manual function, or manual performance. A pooled review of previous research revealed that VRBMT did not significantly alter motor function in stroke patients. These findings suggest that despite VRBMT's potential benefits, it may not be the best rehabilitation technique for restoring upper limb function in stroke patients. However, previous research's findings supported the viability of mirror treatment as a safe method of enhancing upper extremity function employing the camera, augmented reflection, and virtual reality (10).

The current study concluded that VRBMT was found to be effective in improving manual function and manual dexterity in stroke patients. These findings may be due to less number of studies on VRBMT in stroke patients. Whereas contrasting findings were found in Kiper, et al study that VR interventions had a significantly positive impact on shoulder, wrist, and hand outcomes compared to the control group (18). According to the results of the current study, stroke patients' manual function and dexterity were not improved by VRBMT. Contrasting findings were found in a study published in 2022, that VRMT as a treatment presents promising clinical results in restoring motor skills and the function of the affected upper extremity for chronic stroke patients (15). Contrasting findings were found in another study conducted by Errante, et al. that immersive VR is beneficial to enhance upper limb performance and ADL performance in stroke survivors since it provides a highly engaging and stimulating environment (6). The main advantage is that the immersive paradigm promotes balanced recurrence of the brain since the vestibular organ remains active. Indeed, bilateral brain activation when using immersive virtual feedback contributes to the improved multisensory integration of visual and bilateral proprioceptive signals, leading to better motor learning effects" Thus, immersive VR therapy for early-stage stroke has high therapeutic potential, and no significant difference exists between the effective approaches in terms of functional outcomes (15,8). According to some studies, the duration of therapy is a significant factor that influences outcome in addition to the type of intervention (4). VRMT has more functional benefits when the intervention dosage is increased. Additionally, one of the research shows that functional gains persisted for up to six months beyond the conclusion of the training (10).

The findings of our research align with previous literature that highlighted the potential of virtual VRBMT in stroke rehabilitation. Leong et al. addressed the importance of VR therapies in enhancing stroke patients' performance in activities of daily living and upper extremity function (20). Furthermore, more substantial functional improvements may result from increasing the length and intensity of VR therapy (22). Additionally, Zhang et al. notice that continuing functional benefits after the training period emphasize the VR-based therapy's longterm effectiveness in stroke recovery (32). All things taken into account, our study contributes to the increasing amount of data demonstrating the benefits of virtual reality for improving motor function and aiding in stroke patients' recovery.

The research findings indicate that VRBMT may not produce statistically significant improvements in gross manual dexterity, manual function, or motor performance in stroke patients. Nonetheless, it is important to place these findings in the context of a more extensive

body of research. It is important to place these findings in the context of a more extensive body of research. Furthermore, whereas other research has emphasized the significance of goalspecific sensorimotor input and immersive VR settings in encouraging functional recovery poststroke, this study concentrated on gross manual dexterity and manual performance. Variations in the intervention methods, dosage, duration, and the kind of VR technology used, could be the cause of the discrepancy in the results.

Moreover, the debate about the duration of the intervention and how it affects results is consistent with earlier studies suggesting longer intervention durations and higher dosages might result in more notable functional gains. Although we did not find any noteworthy effects, the duration and intensity of the intervention may have an impact on VRBMT's potential efficacy in stroke rehabilitation and a very limited number of RCTs are published on VRBMT.

Whereas this meta-analysis offers insightful information on the efficacy of VRBMT for stroke rehabilitation overall, it is important to take into account a wider array of research that suggests a deeper link between VR treatments and functional results in stroke patients. To better understand how VRBMT improves motor function and aids in stroke recovery, more research should be done on the best intervention strategies and patient selection standards.

The assessment of risk of bias was based on the author's assessment by utilizing the Cochrane tool in the following domains, as indicated in Table 5. The randomization sequence and concealed allocation were generated for all included six studies, which showed a low risk of bias. Similarly, the blinding of participants and personnel and the blinding of outcome assessment were considered for all randomized controlled trials representing a high risk of bias. The low risk of bias was demonstrated among all six studies for selective reporting.

Several limitations of the present review are present which require discussion. First, a small number of the conducted studies might undermine the strength and validity of the results. Second, the unequal length of treatment in each study might explain the differences in SMD scores in stroke patients. Future studies are recommended to address these limitations by conducting a larger number of RCTs with standardized protocols and outcome measures. Moreover, further exploration of optimal VRBMT protocols, including dosage, frequency, and duration, is warranted to elucidate its potential benefits in stroke rehabilitation.

Our meta-analysis concludes that although VRBMT exhibits potential as a novel method for stroke rehabilitation, its effects on gross manual dexterity, manual performance, and upper extremity motor function are not statistically significant. To improve VRBMT protocols and their therapeutic benefits for stroke patients, future research should focus on resolving methodological flaws.

ACKNOWLEDGEMENTS

We would like to thank Ziauddin University for their constant support and guidance.

REFERENCES

1. Arya KN. Underlying neural mechanisms of mirror therapy: Implications for motor rehabilitation in stroke. Neurol India 64(1): 38-44, 2016.

2. Avan A, Hachinski V. Stroke and dementia, leading causes of neurological disability and death, potential for prevention. Alzheimers Dement 17(6):1072-1076, 2021.

3. Choi HS, Shin WS, Bang DH. Mirror therapy using gesture recognition for upper limb function, neck discomfort, and quality of life after chronic stroke: a single-blind randomized controlled trial. Medical science monitor: Int Med J Exp and Clin Res 25:3271–3278, 2019.

4. da Silva Jaques E, Figueiredo AI, Schiavo A, Loss BP, da Silveira GH, Sangalli VA, da Silva Melo DA, Xavier LL, Pinho MS, Mestriner RG. Conventional Mirror Therapy versus Immersive Virtual Reality Mirror Therapy: The Perceived Usability after Stroke. Stroke Res Treat 2023:1-8, 2023.

5. Ekstrand E, Lexell J, Brogårdh C. Test− retest reliability and convergent validity of three manual dexterity measures in persons with chronic stroke. PM&R 8(10):935-943, 2016.

6. Errante A, Saviola D, Cantoni M, Iannuzzelli K, Ziccarelli S, Togni F, Simonini M, Malchiodi C, Bertoni D, Inzaghi MG, Bozzetti F. Effectiveness of action observation therapy based on virtual reality technology in the motor rehabilitation of paretic stroke patients: a randomized clinical trial. BMC Neurol 22(1):109, 2022.

7. Farooq A, Venketasubramanian N, Wasay M. Stroke care in Pakistan. Cerebrovasc Dis Extra 11(3):118-121, 2021.

8. Hao J, Yao Z, Harp K, Gwon DY, Chen Z, Siu KC. Effects of virtual reality in the early-stage stroke rehabilitation: A systematic review and meta-analysis of randomized controlled trials. Physiother Theory Pract 39(12):2569-2588, 2023.

9. Hashmi M, Khan M, Wasay M. Growing burden of stroke in Pakistan: a review of progress and limitations. Int J Stroke 8(7):575-581, 2013.

10. Heinrich C, Morkisch N, Langlotz T, Regenbrecht H, Dohle C. Feasibility and psychophysical effects of immersive virtual reality-based mirror therapy. J Neuroeng Rehabil 19(1):107, 2022.

11. Hsu HY, Kuo LC, Lin YC, Su FC, Yang TH, Lin CW. Effects of a virtual reality–based mirror therapy program on improving sensorimotor function of hands in chronic stroke patients: a randomized controlled trial. Neurorehabil Neural Repair 36(6):335-345, 2022.

12. In TS, Jung KS, Lee SW, Song CH. Virtual reality reflection therapy improves motor recovery and motor function in the upper extremities of people with chronic stroke. J Phys Ther Sci 24(4):339-343, 2012.

13. Israely S, Leisman G, Carmeli E. Improvement in arm and hand function after a stroke with task-oriented training. Case Reports 1-7, 2017.

14. Jafar TH. Blood pressure, diabetes, and increased dietary salt associated with stroke–results from a communitybased study in Pakistan. J Hum Hypertens 20(1):83-85, 2006.

15. Jin M, Pei J, Bai Z, Zhang J, He T, Xu X, Zhu F, Yu D, Zhang Z. Effects of virtual reality in improving upper extremity function after stroke: a systematic review and meta-analysis of randomized controlled trials. Clin Rehabil 1-124, 2022.

16. Kamal AK, Itrat A, Murtaza M, Khan M, Rasheed A, Ali A, Akber A, Akber Z, Iqbal N, Shoukat S, Majeed F. The burden of stroke and transient ischemic attack in Pakistan: a community-based prevalence study. BMC Neurol 9:1-1, 2009.

17. Kim K, Jung H, Di Giovanna E, Jun TJ, Kim YH. Increased risk of ischemic stroke associated with elevated gamma-glutamyl transferase level in adult cancer survivors: a population-based cohort study. Scientific Reports 13(1):16837, 2023.

18. Kiper P, Godart N, Cavalier M, Berard C, Cieślik B, Federico S, Kiper A, Pellicciari L, Meroni R. Effects of Immersive Virtual Reality on Upper-Extremity Stroke Rehabilitation: A Systematic Review with Meta-Analysis. J Clin Med 13(1):146, 2023.

19. Kuriakose, D. and Xiao, Z., 2020. Pathophysiology and treatment of stroke: present status and future perspectives. Int. J. Mol. Sci 21(20):1-24, 2020.

20. Leong SC, Tang YM, Toh FM, Fong KN. Examining the effectiveness of virtual, augmented, and mixed reality (VAMR) therapy for upper limb recovery and activities of daily living in stroke patients: A systematic review and meta-analysis. J Neuroeng Rehabil 19(1):93, 2022.

21. Lin CW, Kuo LC, Lin YC, Su FC, Lin YA, Hsu HY. Development and testing of a virtual reality mirror therapy system for the sensorimotor performance of upper extremity: A pilot randomized controlled trial. IEEE 9:14725- 14734, 2021.

22. Mekbib DB, Zhao Z, Wang J, Xu B, Zhang L, Cheng R, Fang S, Shao Y, Yang W, Han J, Jiang H. Proactive motor functional recovery following immersive virtual reality–based limb mirroring therapy in patients with subacute stroke. Neurotherapeutics 17(4):1919-1930, 2020.

23. Mutai H, Furukawa T, Nakanishi K, Hanihara T. Longitudinal functional changes, depression, and healthrelated quality of life among stroke survivors living at home after inpatient rehabilitation. Psychogeriatrics 16(3):185-190, 2016.

24. Navalta JW, Stone WJ, Lyons TS. Ethical Issues Relating to Scientific Discovery in Exercise Science. Int J Exerc Sci 12(1): 1-8, 2019.

25. Roby-Brami A, Jarrasse N, Parry R. Impairment and compensation in dexterous upper-limb function after stroke. From the direct consequences of pyramidal tract lesions to behavioral involvement of both upper-limbs in daily activities. Front Hum Neurosci 15:662006, 2021.

26. Shaikh HA, Hussain F, Kumar D. Effects of Virtual Reality Therapy on the Balance and Health-Related Quality of Life of Patients With Stroke: A Systematic Review. J Mod Rehabil 14(1):1-0, 2020.

27. Sherin A, Ul-Haq Z, Fazid S, Shah BH, Khattak MI, Nabi F. Prevalence of stroke in Pakistan: Findings from Khyber Pakhtunkhwa integrated population health survey (KP-IPHS) 2016-17. Pak J Med Sci 36(7):1435, 2020.

28. Sip P, Kozłowska M, Czysz D, Daroszewski P, Lisiński P. Perspectives of motor functional upper extremity recovery with the use of immersive virtual reality in stroke patients. Sens 23(2):712, 2023.

29. Teasell R, Salbach NM, Foley N, Mountain A, Cameron JI, Jong AD, Acerra NE, Bastasi D, Carter SL, Fung J, Halabi ML. Canadian stroke best practice recommendations: rehabilitation, recovery, and community participation following stroke. Part one: rehabilitation and recovery following stroke; update 2019. Int J Stroke 15(7):763-788, 2020.

30. Wen X, Li L, Li X, Zha H, Liu Z, Peng Y, Liu X, Liu H, Yang Q, Wang J. Therapeutic role of additional mirror therapy on the recovery of upper extremity motor function after stroke: a single-blind, randomized controlled trial. Neural Plast 2022:1-9, 2022.

31. Yew KS, Cheng EM. Diagnosis of acute stroke. Am Fam Physician 91(8):528-536, 2015.

32. Zhang Q, Fu Y, Lu Y, Zhang Y, Huang Q, Yang Y, Zhang K, Li M. Impact of virtual reality-based therapies on cognition and mental health of stroke patients: systematic review and meta-analysis. J Med Internet Res 23(11):e31007, 2021.

