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April, 2011

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Stroke published online Apr 7, 2011;

DOI: 10.1161/STROKEAHA.110.605451

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ISSN: 1524-4628

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Virtual Reality in Stroke Rehabilitation

A Meta-Analysis and Implications for Clinicians

Gustavo Saposnik, MD, MSc, FAHA; Mindy Levin, PT, MSc, PhD; for the Stroke Outcome Research Canada (SORCan*) Working Group

Background and Purpose—Approximately two thirds of stroke survivors continue to experience motor deficits of the arm resulting in diminished quality of life. Conventional rehabilitation provides modest and sometimes delayed effects. Virtual reality (VR) technology is a novel adjunctive therapy that could be applied in neurorehabilitation. We performed a meta-analysis to determine the added benefit of VR technology on arm motor recovery after stroke.

Methods—We searched Medline, EMBASE, and Cochrane literature from 1966 to July 2010 with the terms “stroke,” “virtual reality,” and “upper arm/extremity.” We evaluated the effect of VR on motor function improvement after stroke.

Results—From the 35 studies identified, 12 met the inclusion/exclusion criteria totaling 195 participants. Among them, there were 5 randomized clinical trials and 7 observational studies with a pre-/postintervention design. Interventions were delivered within 4 to 6 weeks in 9 of the studies and within 2 to 3 weeks in the remaining 3. Eleven of 12 studies showed a significant benefit toward VR for the selected outcomes. In the pooled analysis of all 5 randomized controlled trials, the effect of VR on motor impairment (Fugl-Meyer) was OR=4.89 (95% CI, 1.31 to 18.3). No significant difference was observed for Box and Block Test or motor function. Among observational studies, there was a 14.7% (95% CI, 8.7%–23.6%) improvement in motor impairment and a 20.1% (95% CI, 11.0%–33.8%) improvement in motor function after VR.

Conclusions—VR and video game applications are novel and potentially useful technologies that can be combined with conventional rehabilitation for upper arm improvement after stroke. (*Stroke*. 2011;42:00-00.)

Key Words: outcomes ■ randomized controlled trials ■ rehabilitation ■ stroke recovery ■ virtual reality

Stroke is a devastating disease for patients and their families and a leading cause of adult disability. The risk of stroke increases steeply with age; thus, with the aging of the population, an increase in the prevalence of stroke is expected.^{1,2} Between 55% and 75% of survivors continue to experience motor deficits associated with reduced quality of life.^{3,4} Consequently, with the aging population, more individuals are expected to face the challenge of managing diminished function after stroke.^{2,5} Current clinical practice guidelines for stroke rehabilitation are based on increasing evidence from basic science and clinical studies of the remarkable potential for brain remodeling due to neuroplasticity after neurological injury.^{4,6,7} Specifically, recent studies have suggested that training has to be challenging, repetitive, task-specific, motivating, salient, and intensive for neuroplasticity to occur.⁷ However, current resources are unable to fulfill the intensity requirement for optimizing postinjury neuroplasticity.⁸ Although standard rehabilitation (ie, physiotherapy and occupational therapy) helps improve motor function after stroke, only modest benefits have been shown

to date. Some of the limitations of conventional rehabilitation approaches are outlined in Table 1.^{5,9,10} The head-to-head comparison of conventional rehabilitative approaches (ie, neurodevelopmental techniques, proprioceptive neuromuscular facilitation, or motor relearning) has shown no significant differences between treatment approaches in functional outcomes in stroke survivors.^{9,11} The shortage of rehabilitation providers and resources in different regions has limited the provision of adequate and appropriate rehabilitation services to stroke survivors.^{5,10} As a result of the limitations of conventional rehabilitation, novel strategies targeting motor skill development and taking advantage of the elements enhancing experience-dependent plasticity⁷ have recently emerged, including activities using robotics and virtual reality (VR) technology.^{9,12,13}

VR is a computer-based technology that allows users to interact with a multisensory simulated environment and receive “real-time” feedback on performance. VR exercise applications have the potential to apply relevant concepts of neuroplasticity (ie, repetition, intensity, and task-oriented training of the paretic extremity).⁹ VR applications range

Received October 12, 2010; final revision received November 8, 2010; accepted November 29, 2010.

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The online-only Data Supplement is available at <http://stroke.ahajournals.org/cgi/content/full/STROKEAHA.110.605451/DC1>.

*www.sorcan.ca.

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Stroke is available at <http://stroke.ahajournals.org>

DOI: 10.1161/STROKEAHA.110.605451

Table 1. Limitations of Conventional Rehabilitation^{9,11}

Time-consuming
Labor- and resource-intensive
Dependent on patient compliance
Limited availability depending on geography
Modest and delayed effects in some patients
Requires transportation to special facilities
Initially underappreciated benefits by stroke survivors
Requires costs/insurance coverage after the initial phase of treatment

from nonimmersive to fully immersive depending on the degree to which the user is isolated from the physical surroundings when interacting with the virtual environment.¹² Also classified as VR are a variety of nonimmersive video game systems developed by the entertainment industry for home use, making this technology less costly and more accessible to clinicians and individuals. Several of these games have been adopted by clinicians as rehabilitation interventions although they have not been especially designed to meet rehabilitation goals. In the present study, we reviewed the literature and completed a meta-analysis to evaluate the effectiveness of VR applications including commercial video game systems for upper limb functional recovery after stroke.

Methods

We aimed to include articles published in MEDLINE, EMBASE, and Cochrane Review from 1966 to July 2010.

Eligibility Criteria

The search strategy was set to include both clinical trials and observational studies on the use any VR system in the rehabilitation of the upper extremity of patients who had acute, subacute, or chronic stroke.

Exclusion Criteria

Studies were excluded if they were not carried out on humans, the intervention targeted lower extremity rehabilitation, or did not provide information on the outcome of interest. We also excluded case reports or small case series including <3 patients.

Search Strategy

We searched MEDLINE (PUBMED search engine), EMBASE, and the Cochrane library. Search included the following terms: "stroke," "virtual reality," "upper extremity," "upper arm," or "upper limb."

Data Reviews

Two independent reviewers (M.L. and G.S.) screened the retrieved abstracts for eligibility according to their relevance. Inconsistencies were resolved through discussion until a consensus was reached.

Outcome Measures

The primary outcome was improvement of Fugl-Meyer, a measurement of motor impairment. Secondary outcomes included improve-

Table 2. Virtual Reality in Neurorehabilitation of the Upper Extremity After Stroke: Study Characteristics

Author	Design	No.	Age Range, years	Time Since Stroke Onset	Type of VR	Intervention
Holden et al (2002) ¹⁵	Pre/post	9	26–68	>6 mo	Nonimmersive (Virtual teacher)	1 h/d, 3 d a week×20–30 sessions
Boian et al (2002) ¹⁶	Pre/post	4	58–72	1–4 y	Nonimmersive (CyberGlove and a Rutgers Master, Immersion Corp, San Jose, CA)	2 h/d, 5 d a week, 3 wk
Piron et al (2003) ¹⁷	RCT	VR=12 CR=12	NA	<3 mo	Nonimmersive (VR Motion, VRmotion Ltd, Padova, Italy)	1 h/d, 5 d a week, 5–7 wk
Piron et al (2005) ¹⁸	Pre/post	50	58 (mean)	>6 mo	Nonimmersive (VR Motion, VRmotion Ltd, Padova, Italy)	1 h/d, 5 d a week, 4 wk
Jang et al (2005) ¹⁹	RCT	VR=5 Control=5	43–68	>6 mo	Immersive (IREX, GestureTek technologies, Toronto, Canada)	1 h/d, 5 d a week, 4 wk
Merians et al (2006) ²⁰	Pre/post	8	46–81	1–4 y	Nonimmersive (CyberGlove and a Rutgers Master, Immersion Corp., San Jose, CA)	2–2.5 h/d, 13 d, 3 wk
Broeren et al (2007) ²¹	Pre/post	5	53–63	>6 mo	Immersive (Reaching APE and Crystal Eyes)	45 min/d, 3 d a week, 5 wk
Fischer et al (2007) ²²	RCT	CO=5 PO=5 Control=5	32–88	1–38 y	Immersive (Glasstrom, Sony Electronics, Tokyo/CAVE, VRCO, Virginia Beach)	60 min, 18 sessions, 6 wk
Yavuzer et al (2008) ²³	RCT	VR=10 Sham VR=10	61 (mean)	<12 mo	Immersive (Playstation EyeToy, Sony Entertainment, Tokyo, Japan)	30 min/d, 5 d a week, 4 wk
Kamper et al (2010) ²⁴	Pre/post	VR+device=7 VR control=7	54 (mean) 57 (mean)	>6 mo	Non-Immersive (PneuGlove, Vinyl Technology, Inc, Monrovia, CA)	60 min×3 d a week, 6 wk
Yong et al (2010) ²⁵	Pre/post	16	65 (mean)	< 3 mo	Nonimmersive (Wii, Nintendo, Tokyo, Japan)	30 min×6 sessions within 4 wk
Saposnik et al (2010) ²⁵	RCT	VR+CR=10 RA+CR=10	41–83	<3 mo	Nonimmersive (Wii, Nintendo, Tokyo, Japan)	60 min×8 sessions within 2 wk

RCT indicates randomized controlled trial; VR, virtual reality; CR, conventional rehabilitation; CO, cable orthosis; PO, pneumatic orthosis; RA, recreational activities.

Table 3. Virtual Reality in Neurorehabilitation of the Upper Extremity After Stroke: Outcome Measures

Author	Time Since Stroke Onset	Total No. of Sessions	Outcome Measures	Findings
Holden et al (2002) ¹⁵	Chronic	20–30 sessions	FM, WMFT	Post-training improvement FM 15%, time improvement in WMFT 24%, improvement in total WMFT 31%
Boian et al (2002) ¹⁶	Chronic	15 sessions	JTHF	Significant improvement in computerized measure of thumb range, finger speed, 23%–28% improvement in JTHF
Piron et al (2003) ¹⁷	<3 months	25–35 sessions	FM, FIM	Improvement in FM 20.2% (VR), 11.3% (control); both groups showed a significant improvement at follow-up Improvement in FIM 12.4% (VR), 9.3% (control); both groups showed a significant improvement at follow-up No significant difference found in FM and FIM between groups
Piron et al (2005) ¹⁸	Chronic	20 sessions	FM, FIM	Improvement after training FM 15%, FIM 6%, and mean duration of 18% (all $P<0.05$)
Jang et al (2005) ¹⁹	Chronic	20 sessions	FM, BBT, MFT	Improvement in BBT 15.4% (VR) vs 10% (control; $P<0.05$) Improvement in FM 13.7% (VR) vs 3.8% (control) ($P<0.05$) Improvement in Manual Function test 10% (VR) vs 0% (control)
Merians et al (2006) ²⁰	Chronic	13 sessions	JTHF	Postintervention improvement in range of motion 19.7% ($P<0.005$), velocity 9.8% ($P<0.007$), and JTHF 15% (0.008); similar degree of improvement were 1 wk postintervention
Broeren et al (2007) ²¹	Chronic	15 sessions	Kinematics, BBT, AMPS	Unilateral dexterity improved 11% post-test and 17% at follow-up Grip strength: improvement 13%–57% of the mean score compared with a age-/sex-matched healthy control subjects No significant difference was observed in BBT and AMPS
Fischer et al (2007) ²²	Chronic	18 sessions	WMFT, FM, BBT	Improvement in WMFT 7.2% (control), 2.2% (CO), 14.1% (PO; $P=0.02$) Improvement in FM 12% (control), 14.3% (CO), –5.3% (PO) BBT 0→3 (control), 3→5 (CO), 4→3 (PO)
Yavuzer et al (2008) ²³	Subacute/chronic	20 sessions	Brunnstrom, FIM	Significant difference in the change of motor performance (Brunnstrom scale) between groups ($P<0.009$) and FIM self-care ($P<0.001$) Improvement in motor performance (baseline to postintervention) within group 47.4% (VR), 3.7% (control) Improvement in FIM (baseline to postintervention) within group 20% (VR), 4.2% (control)
Kamper et al (2010) ²⁴	Chronic	18 sessions	FM, BBT	Improvement in FM 12.2% (VR) vs 16.5% (VR globe; $P<0.05$) Improvement in grip strength 12.3% (VR) vs 3.9% (VR globe; $P<0.05$) Improvement in BBT 3.9% (VR) vs 20.7% (VR globe; $P<0.05$); similar findings were observed at follow-up 4 wk postintervention
Yong et al (2010) ²⁵	Subacute	6 sessions	FM, MFT, MAS	Improvement in FM 12.2% ($P=0.007$), Motricity index 6.6% ($P=0.031$), and MAS 20.6% ($P=0.32$)
Saposnik et al (2010) ²⁶	Subacute	8 sessions	WMFT, BBT, SIS	Improvement within VR group in WMFT (35.5%), BBT (26%), and grip strength (29%) Improvement within the control group in BBT (49%) and SIS hand (17%); no improvement observed in WMFT, grip strength; there was a 35% improvement in WMFT (–7; 95% CI –14.5 to –0.2) favoring the VR group after adjustment for differences in baseline characteristics

FM indicates Fugl-Meyer Arm Scale; WMFT, Wolf Motor Function Test; JTHF, Jebsen Test of Hand Function; FIM, Functional Independence Measure; BBT, Box and Blocks Test; MFT, Manual Function Test; AMPS, Assessment of Motor and Process Skills; MAS, Modified Ashworth Scale; SIS, Stroke Impact Scale; VR, virtual acuity; CO, cable orthosis; PO, pneumatic orthosis.

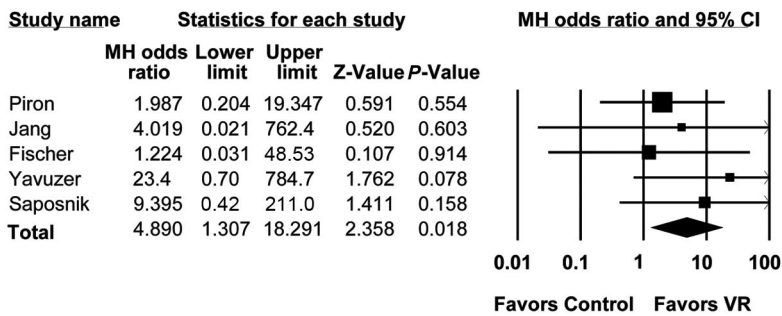
ment in motor function measured as Wolf Motor Function Test (WMFT), Box and Block Test, and Jebsen-Taylor Hand Function Test.

Analysis

The Comprehensive-Meta-analysis software package (Biostat Inc 2006) was used for the meta-analysis. Differences in outcomes measures

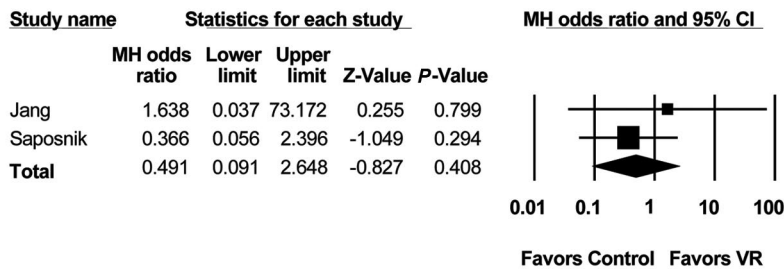
between groups or from baseline are reported in relative terms as provided by the authors or estimated from raw data. We assessed heterogeneity using χ^2 test and I^2 .¹⁴ A separate analysis was completed for randomized controlled trials (RCTs) and observational studies due to methodological differences. For RCTs, we evaluated the pooled treatment effect (Mantel-Haenszel OR) by using random-effect models to reduce the effects of heterogeneity between studies. For observational

A RCT Outcome: Improvement of Motor Impairment



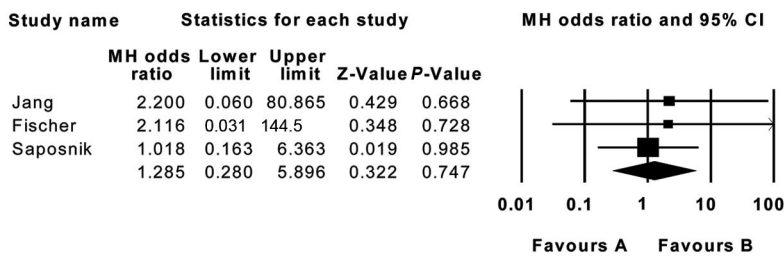
Heterogeneity: $X^2= 2.087$, $df=4$ ($p=0.72$) $I^2= 0\%$

B RCT Outcome: Box & Block test



Heterogeneity: $X^2= 0.481$, $df=1$ ($P=0.488$) $I^2= 0\%$

C RCT Outcome: Motor function (Wolf motor function test, manual function)



Heterogeneity: $X^2= 0.201$, $df=2$ ($P=0.90$) $I^2= 0\%$

Figure 1. Meta-analysis of RCTs using VR systems in upper extremity impairment (A) and motor function (B, C). RCTs indicates randomized controlled trials; VR, virtual reality.

studies, we used standardized mean difference and 95% CIs to represent the magnitude of the improvement compared with baseline. For all analyses, $P<0.05$ was considered statistically significant (see details in the Supplement file; <http://stroke.ahajournals.org>).

Results

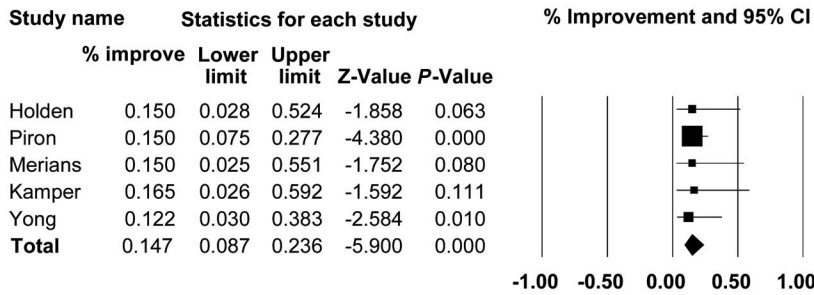
There were 35 articles published in Medline combining the selected terms. There were no studies published in EMBASE or in the Cochrane Collaboration. Twelve studies met the inclusion criteria.^{15–26} Among them, there were 5 RCTs^{18,19,22,23,26} and 7 observational studies with a pre-/postintervention design.^{15–17,20,21,23,25} Table 2 summarizes the studies' characteristics and outcomes. Studies included VR ($n=9$) and commercial video game ($n=3$) interventions. Only 3 studies targeted patients with acute/subacute stroke^{18,25,26}; the remaining 9 included patients with chronic stroke (>6 months). Age ranged from 26 to 88 years old. Two thirds ($n=8$) of the interventions used nonimmersive VR systems (Virtual teacher, Cyberglobe, VR Motion, Pneumoglobe,

Wii). Among the RCTs, there were 3 studies using immersive VR (eg, Glasstrom, IREX, Playstation EyeMotion)^{19,22,23} and 2 applying nonimmersive systems (eg, VR Motion, Wii).^{18,26}

Interventions were delivered within 4 to 6 weeks in most of the studies ($n=9$). The duration of the sessions were 1 hour in most of the studies ($n=7$; range, 30 minutes to 2.5 hours/session). The most commonly used outcome measure was the Fugl-Meyer ($n=7$) followed by the Box and Block Test ($n=4$), the WMFT ($n=3$), and the Functional Independence Measure ($n=3$). Eleven of 12 studies showed a significant benefit toward VR for the selected outcomes (Fugl-Meyer, WMFT, Functional Independence Measure; Table 3).

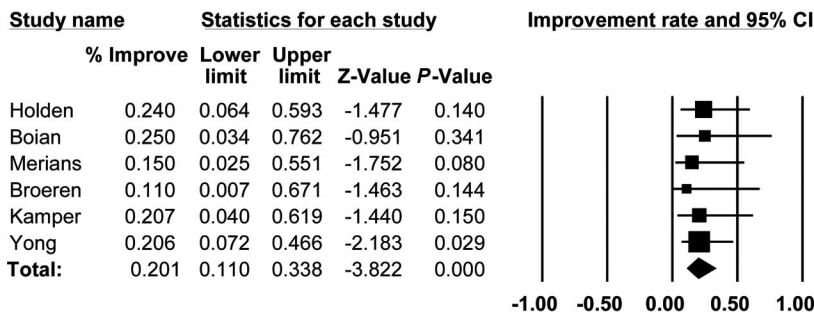
At the Body Structure and Function level of the International Classification of Functioning,²⁷ major outcomes were Fugl-Meyer scores and measures of arm movement speed, range of joint motion, and force. At this level, improvements ranged from 13.7% to 20% compared with 3.8% to 12.2% for control groups. Similarly at the activity level of the Interna-

A Observational studies: Motor Impairment



Heterogeneity: $\chi^2=0.102$, $df=4$ ($P=0.99$) $I^2=0\%$

B Observational studies: Motor function



Heterogeneity: $\chi^2=0.52$, $df=5$ ($P=0.99$) $I^2=0\%$

Figure 2. Meta-analysis of observational studies using VR systems in upper limb impairment (A) and motor function (B). VR indicates virtual reality.

tional Classification of Functioning, outcomes such as WMFT, the Jebson-Taylor Hand Function Test, and the Box and Block Test showed increases of 14% to 35.5% for VR applications compared with 0% to 49% for control groups. After all 5 RCTs were pooled (Figure 1), the effect of VR on motor impairment was OR=4.89(95% CI, 1.31 to 18.3; $P<0.02$; Figure 1A). There was no significant effect on the Box and Block Test (Figure 1B; 2 RCTs; OR, 0.49; 95% CI, 0.09 to 2.65; $P=0.41$) or WMFT (Figure 1C; 3 RCTs; OR, 1.29; 95% CI, 0.28 to 5.90; $P=0.74$). Among observational studies (Figure 2), the effect of VR on motor impairment (percent improvement from baseline) was 14.7% (95% CI, 8.7% to 23.6%; $P<0.001$; Figure 2A) after either type of VR. The effect on motor function (Jebson-Taylor Hand Function Test, WMFT, Motor Activity Scale) was 20.1% (95% CI, 11.0% to 33.8%; $P<0.001$; Figure 2B). The sensitivity analysis using fixed-effect models showed no difference in the significance of the treatment effect for any of the outcomes. There was no evidence of publication bias for the assessed outcomes as per the visual (see Supplemental Figure I) or statistical methods (Egger $P=0.639$).

Discussion

Rehabilitation is an essential component to any program aimed at improving motor function in stroke survivors.^{4,11} Novel strategies are becoming available to overcome the modest benefits of conventional rehabilitation.^{9,28} The current paradigm for assessing innovative interventions in rehabilitation should include an evaluation of function, activities, and social participation.^{27,29} Different tools (eg, scales) are avail-

able to assess each domain. In a recent systematic review comparing different approaches in stroke rehabilitation, constraint-induced movement therapy was more effective than conventional rehabilitation in patients within 3 to 9 months from stroke.^{9,29} Interestingly, VR applications were not included.⁹

In the present meta-analysis, we found 12 studies and 5 RCTs. Eleven of 12 studies showed a benefit for the primary outcome. There was a significant 4.9 higher chance of improvement in motor strength for patients randomized to VR systems. Formal testing did not identify any substantial heterogeneity among trial findings. Similarly, there was a significant 15% improvement in motor impairment and 20% improvement in motor function outcomes from the pooled observational studies.

There Were No Large Studies Comparing the Benefit of the Combination of Conventional Therapy and VR Technology

In a previous literature review completed in 2007 by members of our group examining studies using VR systems applied to the arm as a rehabilitation strategy after stroke, there were only 5 publications, 2 RCTs and 3 observational studies.¹² Meta-analysis was not completed. Because VR systems are now more available and more widely used, further analysis from the clinician’s perspective is warranted.

However, there are several differences in the population target, design, VR systems, and interventions. For example, some studies compared an intervention plus conventional physical therapy versus conventional physical therapy alone,

which by necessity allowed for more rehabilitation time in the experimental group.⁹ This creates a bias in favor of the new intervention because the intensity and frequency of rehabilitation per se is known to directly and beneficially affect functional outcomes. Moreover, there was a broad variety of outcome measures. Some studies focused on single rather than multiple dimensions (eg, motor impairment, activities, social participation/quality of life). For instance, the main outcome measure was motor function using WMFT or the Box and Block Test in 6 of 12 studies, and only 1 included social participation/quality of life (Stroke Impact Scale). Improvement in activities of daily living (eg, Barthel index; 0/12) or social participation/quality (1/12) of life were not included in the majority of the studies.

The limited number of studies is likely due to the only recent availability of this novel technology and, therefore, subject to potential publication bias. For example, in the 1990s, most VR systems were limited to use in research laboratories. More recently, the entertainment industry has facilitated a significant growth in the number of rehabilitation applications. In fact, 6 of 12 studies included in the present meta-analysis were published in the last 3 years.

What Are the Potential Implications for Clinicians?

Recovery of motor skill depends on neurological recovery, adaptation, and learning new strategies and motor programs.^{7,9} VR systems apply relevant concepts for driving neuroplasticity (ie, repetition, intensity, and task-oriented training of the paretic extremity)⁹ and lead to benefits in motor function improvement after stroke.¹² This is possible due to cortical reorganization and rewiring in the injured brain (brain plasticity).^{6,19} The use of VR showed practice-dependent enhancement of the affected arm through the facilitation of cortical reorganization. This process may be facilitated by the provision of multisensorial (visual, auditory, and tactile) feedback of some VR systems (eg, Wii, Kinect, Playstation).¹⁹ The duration and intensity of the rehabilitation strategy are important factors in its effectiveness.⁹ The present analysis suggests that VR and video game applications may be promising strategies to increase the intensity of treatment and to promote motor recovery after stroke. However, not all patients would be eligible for this technology. Most studies included patients with mild to moderate stroke and did not assess the more challenging severely affected patients. Future studies may help determine whether the combination of VR with conventional physical and occupational therapy enhances stroke rehabilitation.

Stroke rehabilitation is rapidly evolving. Novel approaches including the use of VR systems may help improve motor impairment, activities, and social participation. The primary purpose of this review is to present information rather than to offer advice or recommendations. Larger multicenter randomized trials are needed before making conclusions that might influence clinical practice. The completion of well-designed RCTs will ultimately advance knowledge about the optimal rehabilitation strategy for patients with a disabling stroke.

Sources of Funding

G.S. is supported by the Clinician Scientist Award from Heart and Stroke Foundation Ontario (HSFO).

Disclosures

G.S. is the Principal Investigator of EVREST, a multicentre, randomized, clinical trial comparing the efficacy of virtual reality using the Nintendo Wii gaming technology versus recreational therapy in stroke patients receiving conventional neurorehabilitation. The study is supported by Heart and Stroke Foundation following a competitive grant application.

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