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STROKE REHABILITATION (RD ZOROWITZ, SECTION EDITOR)

Virtual Reality for Sensorimotor Rehabilitation Post-Stroke: The Promise and Current State of the Field

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Abstract Developments over the past 2 years in virtual reality (VR) augmented sensorimotor rehabilitation of upper limb use and gait post-stroke were reviewed. Studies were included if they evaluated comparative efficacy between VR and standard of care, and or differences in VR delivery methods; and were CEBM (center for evidence based medicine) level 2 or higher. Eight upper limb and two gait studies were included and described using the following categories hardware (input and output), software (virtual task and feedback and presentation) intervention (progression and dose), and outcomes. Trends in the field were commented on, gaps in knowledge identified, and areas of future research and translation of VR to practice were suggested.

Keywords Stroke · Rehabilitation · Virtual reality · Virtual environment · Gait · Walking · Mobility · Balance · Upper extremity · Arm · Hand · Robotics · Haptics · Immersive · Semi-immersive

Introduction

The introduction of virtual reality (VR) augmented sensorimotor rehabilitation was heralded as a therapy that promised ecologically valid, intensive task specific training [1]. It was purported to provide multi-sensory training that would transfer from the virtual world to the real world [2]. Additionally, it was suggested that VR could deliver training intensity (repetitions and duration) associated with neuroplasticity and positive behavioral adaptations [3] because it was particularly well suited to very high training doses [4, 5]. Early reviews of the field have shown that promise to be partially met [6, 7]. Virtual reality technology and its application to motor rehabilitation have been described elsewhere [5, 8] and will not be the focus of this paper.

The study of virtual reality-enhanced rehabilitation has a short life of approximately a decade. The field has matured. There are two alternating bi-annual international conferences, International Conference on Virtual Reality Rehabilitation http://virtual-rehab.org/2013/ (originally the Workshop on Virtual Reality originated by Drs. Burdea and Thalman) and the International Conference on Disability Virtual Reality and Associated Technologies www.icdvrat.reading.ac.uk/ (organized by Dr. Sharkey). Both of these meetings publish proceedings. Recently members of both groups have formed the International Society for Virtual Reality (www.isvr.org).

Work in the field has merged engineering, cognitive neuroscience, biomechanics and rehabilitation sciences. There is an arc from development to validation and subsequent efficacy testing. Early in the field's development papers were primarily technical with single case reports and descriptive studies [9, 10]. The first randomized controlled trial on walking recovery was published in 2004 [11] and the field's progress was reviewed with a focus on upper limb (UL) rehabilitation [12], more globally [4], with emphasis on video capture systems [13] and in a Cochrane review [7•]. The purpose of this paper is to review and

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comment on the randomized controlled trials (RCTs) published since the stroke and on virtual reality Cochrane review [7•], with an emphasis on evidence of VR technologies' efficacy for sensorimotor rehabilitation of the upper limb and gait post-stroke, and translation to practice. Further, we will speculate on research to advance the science of the field and future directions for the integration of VR in stroke rehabilitation.

Method

A Medline search using the terms "virtual reality" and "stroke" for the period of March 2010 to the present was performed. This time period was selected to include articles that were more recent than those examined in stroke and virtual reality Cochrane review [7•]. Both authors independently reviewed the citations and selected articles that met the following criteria: were RCTs that compared standard of care to virtual reality, or compared different delivery methods in VR. The inclusion criteria of the latter, distinguishes this paper from the recent Cochrane review. Studies were excluded if they did not meet the CEBM level of evidence three or higher (http://www.cebm.net/), had a mechanistic or validation of technology focus or used off-the-shelf video games. Video games are often grouped with virtual reality studies, but for purposes of this paper they were excluded. Agreement between independent reviews was determined by consensus.

The search yielded 50 articles of which ten met the inclusion criteria. Information from the articles was extracted using the following categories:

Sample	*Number* of participants, time post-stroke (in months), *motor function* and *cognition.*
Hardware	(1) *Interface* collecting movement data (input): such as a camera, sensorized glove or robotic exoskeleton, from the subject. (2) Equipment *presenting (output)* (a) Visual information: such as a computer screen or a head mounted display, and, or, (b) Tactile information (which is used to augment the visual and auditory stimuli, presented with haptics, (such as an exoskeleton) and, or, real contact (such as mixed reality systems interacting with real objects) to the subject.
Simulation	(1) The virtual *task* that participants perform. (2) The *feedback* provided to augment motor learning: (a) knowledge of results (KR) which is information related to achievement of the movement goal and (b) Knowledge of Performance (KP) which is information about subject's movement strategy [14]. (3) The visual *presentation* either in two or three dimensions and *perspective* first or third person.
Comparison	*Experimental* (typically VR) and *control* conditions (either standard of care or alternate form to deliver VR).
Intervention	(1) *Dose*: the number of minutes, days and weeks of the intervention. (2) *Progression*: the method used to increase training difficulty Treatment progression was achieved with combinations of hardware, software and clinician inputs. Exercise progression was driven by algorithms, which were implemented in the software or performance information generated by the software, which was then used by clinician to make decisions. Inputs for the algorithms were attributes of motor performance such as speed, accuracy, trajectories, goal attainment, which in turn manipulated the physical properties of the interaction such as: weight, size, speed of objects in a simulation.
Outcomes	Pre-Post testing for all studies and follow-up if available.

Authors independently extracted the data for the UL (GF) and gait studies (JD).

Results

Since the Cochrane review on stroke and virtual reality was published, there have been ten more RCTs on the topic with the majority of these studies addressing rehabilitation of the UL (8) compared to gait and mobility (2). The findings are presented in Tables 1: UL studies comparing VR to standard of care [15••, 16, 17, 18•], Table 2: UL studies comparing VR presentation [19, 20•, 21••, 22], and Table 3: gait studies [23, 24•].

Discussion

In the Cochrane review there were eight studies on the UL and three on gait and mobility. The main finding of that review was the evidence to support the use of VR over standard of care for UL but not gait rehabilitation post-stroke. In this paper we look at comparative efficacy as well, but also at important aspects of technology delivery. It is noteworthy that the Cochrane review covered a period of six years and this paper represents only two-and-a-half-year period. The quantity of the clinical trials in VR research on comparative efficacy and technology delivery continues to progress with a disproportionately larger number of studies on the UL. To provide a perspective on the field, we discuss and comment on each of the elements in the results tables.

Table 1 UL studies comparing VR to standard of care [14, 15••, 16, 17]

References	Sample	Hardware	Simulation	Comparison	Intervention	Pre to post	Pre to retention
Cameriao [15••]	$N = 8$	Input: AnTS tracking system	Task: intercept flying spheres	VR vs. intensive	Dose: all 12 weeks	**UEFMA**	**UEFMA**
Restorative	Age 63 (12)				× 3 days × 20 min	VR 38–60*	VR 38–60
Neurology & Neuroscience	Days post 12 (5)				*Plus*	Control 24–53*	Control 24–55
	UEFMA 38 (12)				In-hospital rehab	**Motricity Index§**	**Motricity Index**
						VR 52–85*	VR 52–90
						Control 43–77*	Control 43–81
	Control	Output: screen	Feedback: KR-game score and speed	OT or non-specific gaming	Progression: algorithm scales task difficulty	**CAHAI§**	**CAHAI***
	$N = 8$					VR 30–84*	VR 30–84
	Age 59 (11)					Control 25–70*	Control 25–78
	Days post 15 (5)		Presentation: 2d			**Barthel Index**	**Barthel Index**
	UEFMA 24 (11)		Avatar first person			VR 42–96*	VR 42–98
						Control 46–94*	Control 46–96
Crosbie [16]	VR	Input: HMD magnetic tracker	Task: reaching and finger/wrist AROM	VR vs. PT delivered facilitation, stretching strengthening UE tasks	Dose: 3 weeks 3 days 45 min Therapist controlled target placement or task speed	**Motricity Index** NS, **ARAT** NS	**Motricity Index** NS, **ARAT** NS
Clinical Rehabilitation	$N = 9$						
	Age 56 (14)						
	Mos. post 10 (6)						
	Mothricity 84 (8)						
	Control	Output: HMD	Feedback: KR: Game score				
	$N = 9$						
	Age 65 (7)						
	Mos. post 12 (8)		Presentation: Immersive 3-D				
	Mothricity 92 (16)		Avatar				
Levin [17]	VR $N = 8$	Input: camera	Task: Soccer goalie, catching flying bird, virtual shopping	VR vs. conventional OT including grasping	Dose: 3 weeks 3 days 45 min	**UEFMA**	**UEFMA**
Neurology & Therapy	Age 58 (15)					VR 40–47	VR 40–46
	Mos. post 31 (14)					Control 42–45	Control 42–48
	UEFMA 40 (14)					**CSI**	**CSI**
						VR 7–6	VR 7–6
						Control 9–9	Control 9–8

Table 1 continued

References	Sample	Hardware	Simulation	Comparison	Intervention	Pre to post	Pre to retention
	Control $N = 6$ Age 60 (15) Mos. post 46 (11) UEFMA 42 (14)	Output: large 2d screen	Feedback: Presentation:semi-immersive mirrored self-view 2d		Progression: not specified	**RPSS** VR 14–15 Control 11–13 **WMFT (FAS)** VR 48–54 Control 50–53 **BBT-NS** **WMFT (s)-NS** **MAL-QOM-NS** **MAL-AOU-NS**	**RPSS** VR 14–14 Control 11–14 **WMFT (FAS)** VR 48–56 Control 50–55 **BBT-NS** **WMFT (s)-NS** **MAL-QOM-NS** **MAL-AOU-NS**
Subramanian [18•] NNR	VR $N = 16$ Age 58 (10) Mos. post 44 (26) UEFMA 42 (15)	Input: Caren system	Task; virtual supermarket for reaching activities Feedback: KR: target acquisition, movement time. KP: trunk excursion	VR: reaching for 6 objects in virtual super-market	Dose: 4 weeks 3 days 45 min	**RPSS (near)*** **RPSS (far)*** **WMFT (FAS)*** **WMFT (s)*** **UEFMA**-NS	**RPSS (near)*** **RPSS (far)*** **WMFT (FAS)*** **WMFT (s)*** **UEFMA**-NS
	Control $N = 16$ Age 60 (11) Mos. post 36 (23) UEFMA 41 (15)	Output VE: rear projection with stereoscopic glasses	Presentation: semi immersive Avatar 2d	Control pointing to 6 Real targets	Progression: not specified		

Mos months, *UEFMA* upper extremity Fugl-Meyer assessment, *HMD* head-mounted display, *KR* knowledge of results, *KP* knowledge of procedure, *min* minute, *AROM* active range of motion, *ARAT* action research arm test, *CSI* composite spasticity index, *RPSS* reaching performance scale for stroke, *WMFT* Wolf motor function test, *MAL* motor activities log, *QOM* quality of movement, *AOU* amount of use

§ Statistically significant between group comparison ($p < .05$), * Statistically significant change ($p < .05$)

Table 2 UL studies comparing VR presentation [18•, 19, 20•, 21••]

Ref	Sample	Hardware	Simulation	Comparison	Intervention	Pre to post	Pre to retention
Hwang [19] Clinical Rehabilitation	Full VR $N = 9$ Age 50 (4) Mos. post 7 (6) UEFMA 41 (4)	Input via Amadeo	Task: firefighting and balloon piloting Feedback: KR: % task completion, # Obstacles avoided, performance time	VR X 4 weeks vs. PROM x 2 weeks then VR X 2 weeks	Dose : 4 weeks 5 days 40 min.	**UEFMA (Distal)** Full VR 19–23 Half VR 18–21 **Grasp (Kg)§** Full VR 15–17 Half VR 14–14 **Pinch (Kg)§** Full VR 2–3 Half VR 2–2	**UEFMA (Distal)§** Full VR 19–23 Half VR 18–21 **Grasp (Kg)§** Full VR 15–17 Half VR 14–14 **Pinch (Kg)§** Full VR 2–3 Half VR 2–2
	Half VR $N = 6$ Age 51 (3) Mos. post 5 (6) UEFMA 39 (6)	Output Vsiual via 2-D Screen Haptics; N/A	KP: hand aperture Presentation: 2d semi immersive Avatar		Progression: therapist controlled target placement	**Finger AROM§** Full VR 57–77 Half VR 52–62 **JTHF§** Full VR 210–143 Half VR 153–105 **MAS**-NS, **SIS**-NS, **NHPT**-NS	**Finger AROM§** Full VR 57–78 Half VR 52–64 **JTHF§** Full VR 210–143 Half VR 153–108 **MAS-NS**, **SIS**-NS, **NHPT**-NS
Abdollahi [20•] IEEE ICORR Proceedings	Experimental $N = 19$ Age 59 (11) Mos. post 7 (6)	Input via WREX and Phantom	Task: gross UE cursor tracking	VR with Error augmented vs. VR with error not augmented	Dose : 2 weeks 3 days 60 min per phase	**Reaching area§** EA > No EA	**Reaching area§** EA > No EA
	UEFMA 30 (12)	Output Visual via 2D screen Haptics via WREX and Phantom	Feedback: KP: visual presentation: 2d Avatar		Progression: therapist controlled target placement	**UEFMA NS** **WMFT** NS **BBT** NS	**UEFMA NS** **WMFT** NS **BBT** NS

Table 2 continued

Ref	Sample	Hardware	Simulation	Comparison	Intervention	Pre to post	Pre to retention
Cameriao [15••]	Camera	Camera Input: AnTS tracking system	Task:	Interfaces	Dose:	**UEFMA**	**UEFMA**
Stroke	$N = 16$	Haptic Input: GRAB system	intercept flying spheres	**Camera** vs. **Haptic**	4 weeks	Camera 35–38*	Camera 35–38*
Note:	Age 68 (11)	EXOSKEL Input: Armeo (Bilateral)	Feedback:		5 days	Haptic 33–37	Haptic 33–39
EXOSKEL = Exoskeleton	Mos. post 55 (10)	All:	KR-game score & speed		35 min	EXOSKEL 36–39	EXOSKEL 36–36*
	UEFMA 35 (11)						**Motricity Index**
							Camera 56–60*
							Haptic 56-59*
							EXOSKEL 53–56*
	Haptic	Output: Screen	Presentation: 2d Avatar	Robot interface vs. EXOSKEL	Progression: algorithm scales task difficulty	**Motricity Index**	**CAHAI**
	$N = 14$	Haptics via GRAB system	first person	Robot (Bilateral Armeo)		Camera 56–59*	Camera
	Age 59 (10)					Haptic 56–59*	37–39
	Mos. post 53 (7)					EXOSKEL 53–58*	Haptic 36–40*
	UEFMA 33 (12)					**CAHAI**	EXOSKEL 35–38*
	EXOSKEL					Camera 37–39*	**Barthel Index**
	$N = 14$					Haptic 36–41*	Camera 89–91*
	Age 59.9 (13)					EXOSKEL 35–39*	Haptic 89–90
	Mos. post 44 (10)					**Barthel Index**	EXOSKEL 90–91
	UEFMA 36 (12)					Camera 89–90*	**BBT**-NS, **MAS**-NS
						EXOSKEL 90–92*	
						BBT-NS, **MAS**-NS	
Connelly [22]	Glove	Input	Task:	**VR + Pneumatic**	Dose	**UEFMA**	**UEFMA**
IEEE EMBC Proceedings	$N = 7$	Glove: Pneumatic glove	shelf and real object reach and grasp	**Glove** vs. **VR with no glove**	6 weeks	Glove 37–43*	Glove 37–43*
	Age 57 (18)	All: Magnetic tracker			3 days	No Glove 38–43*	No Glove 38–44*
	Mos. post 57 (18)				60 min	**BBT**	**BBT**
	UEFMA 37 (3)					Glove 16–20*	Glove
						No	16–19*
						Glove 21–21	No Glove 21–23*
						Palmar Pinch	**Palmar Pinch**
						Glove 26–39*	Glove 26–41*
						No Glove 23–30*	No Glove 23–28*

Table 2 continued

Ref	Sample	Hardware	Simulation	Comparison	Intervention	Pre to post	Pre to retention
	No Glove $N = 7$ Age 54 (10) Mos. post 122 (142) UEFMA 38 (4)	Output: HMD Haptics via Pneumatic Glove	Feedback: not described Presentation: 3D Avatar first person		Progression: therapist scales real object task difficulty Algorithm scales virtual task assistance	**Lateral Pinch**-NS **Grip**-NS	**Lateral Pinch**-NS **Grip**-NS

Mos months, *UEFMA* upper extremity Fugl-Meyer assessment, *HMD* head-mounted display, *KR* knowledge of results, *KP* knowledge of procedure, *min* minute, *AROM* active range of motion, *JTHF* Jebsen-Taylor test of hand function, *MAS* modified Ashworth scale, *SIS* stroke impact scale, *NHPT* nine hole peg test, *BBT* box and blocks test, *CAHAI* Chedoke-Mcmaster hand activity inventory

§ Statistically significant between group comparison ($p \leq .05$), * Statistically significant change ($p \leq .05$)

The *participants* in the studies were typically in the chronic phase (greater than 6 months) post-stroke. The exceptions were Cameriao [15••], who studied acute (4–22 days post) participants in the inpatient setting, and Hwang [19] and Levin [17], who studied sub-acute participants (both less than 3 months).

Cognitive and perceptual characteristics of the participants were mentioned in all studies. Standardized measures of cognition were presented in four studies [16, 17, 18•, 19] but none characterized the cognitive abilities of their sample. Only two studies described a cut-off score on a validated measure of sensory function or perception: Hwang [19], who used the Nottingham Sensory Scale [25], and Crosbie [16], who utilized the mental test [26]. However, neither described their participants' cognitive, perceptual and sensory abilities. The apparent assumption that cognition and perception have an impact on the ability to perform virtual rehabilitation activities is demonstrated by their use as participation criteria in all of these studies. Future characterization of the cognitive, sensory and perceptual abilities of the subjects participating in trials will increase both the external validity and targeted application of VR. It will also reduce the artificial separation between cognitive and motor rehabilitation. Some of this work is already taking place by using VR to address both cognitive and motor impairments for people with PD [27•] and acquired brain injury [28].

Most participants in both UL and gait studies had moderately severe motor control impairments. For the UL studies, moderate severity was measured with scores between 30 and 42 out of 44 points in the upper extremity Fugl Meyer assessment (UEFMA) [29], representing active movements characterized by synergy and minimal manipulation abilities. For the gait studies, lower extremity Fugl-Meyer (LEFM) [27•] scores ranged from 15 to 28 out of 34 points. However, there was great variability in motor severity within studies (standard deviations for three of these studies were larger than 12 points). One study split its sample into moderately and mildly impaired groups, with more impaired subjects making larger magnitude gains with both VR and control interventions [18•]. While better characterized than cognition, the stratification of motor severity in future studies will further aid in selective application of the technology.

The *hardware* interfaces used for both UL and walking systems were either robotic or motion sensing systems. Five of the eight UL studies, and one of the two walking studies, used a motion-sensing interface, while the remaining studies reported work with robotic systems. Neither interface appeared to yield superior motor outcomes. The addition of the sense of touch or haptics was included both UL and gait studies. Four UL systems were enhanced with haptics, three were purely visually based,

Table 3 Gait studies [22, 23]

Citation	Sample	Hardware	Simulation	Comparison	Intervention	Pre-Post	Pre-Retention
Yang [23]	VR $N = 7$ E Age 56.3 (10) Mos. post > 6 Ind. Amb.	Input TM with speed detector	Task; Park walk, path with turns, home activities	20 min walking on TM with VR **vs.** 20 min walking on TM looking out window	Dose: 4 weeks 3 days 40 min	**Sit to Stand** **Center of Pressure§** VR* > Control **Symmetry Index§** VR* > Control*	Not tested
	Control $N = 7$ Age 65.7 (6) Mos. post > 6 Ind. Amb.	Output Visual: projector Haptics: N/A	Presentation: 2D semi immersive Avatar	**Plus (both groups)** 40 min PT (parallel bars, biking, hand function)	Progression : N/A	**Gait** **Paretic Limb Stance Time§** VR* > Control **Paretic Limb Stance COP§** VR* > Control **Quiet Stance** **Center of Pressure-**NS **Symmetry Index**–NS	
Mirelman [24•] Gait and Posture	VR + Robot $N = 8$ Age 61 (10) Mos. post LEFMA 24(3)	Input Robotic interface	Task: air and sea scape navigation through targets	LE training using robotic interface **in VR** vs. LE training using robotic interface **only**	Dose: 4 weeks 3 days 40 min	**Gait Speed (m/s)§** VR + Robot: 0.65–0.80* Robot only: 0.67–68 m/s	**Gait Speed (m/s)§** VR + Robot: 0.65–0.68* Control 0.67–0.68
	Robot only $N = 8$ Age 61 (8) Mos. post LEFMA 22(4)	Output Visual: desktop Haptics: robotic interface	Presentation: 2d semi immersive Avatar		Progression: therapist-controlled difficulty	**Ankle Power (NM/kg)§** VR + Robot: 0.74–0.90* Robot only: 0.5–0.52	**Ankle Power (NM/kg)§** VR + Robot: 0.74–0.94* Robot only: 0.5–0.54

mos months, *Ind Amb* independent ambulation, *LEFMA* lower extremity Fugl-Meyer assessment, *TM* treadmill, *min* minutes, *s* second

§ Statistically significant between group comparison ($p < .05$), * Statistically significant change ($p < .05$)

and one had a mixed reality where subjects interacted with real world objects. Controlled comparisons of interventions providing haptic feedback with similarly presented virtual interventions without haptic feedback were tested in two UL [21••, 22] studies summarized in this article. The UL studies identified a small additive effect in terms of better real world activity level outcomes in subjects performing interventions with haptic feedback. The current literature does not point to robust clinically meaningful activity level outcomes for haptics added to VR systems.

Simulations for both the UL and walking were evenly grouped into two categories: replication of real world tasks such as reaching [18•] and walking [23], or game-based tasks, such as flying a plane with the impaired effector [24•]. For the UL, reaching tasks were performed by retrieving or transporting virtual objects to shelves and or table tops in virtual environments (VEs) that progressed from simple (a shelf) to complex (a supermarket) [17]. The games involved intercepting moving objects [15••, 21••], piloting an avatar through a VE [19], or sport simulations that required interaction with a ball [17]. For walking recovery, simulations were delivered in a variety of environments and similarly were divided into two groups: walking tasks that mimicked the trained tasks [23], and navigation simulations that promoted use of the lower extremities [24•].

Reaching simulations consistently improved reaching abilities [18•, 22], while game-based UL interventions produced less specific outcomes. In the gait studies, there were interesting findings, in that the game-based task coupled with a robotic interface showed a specific transfer of training to the trained distal effector as well as the task of walking [24•], while the walking simulation improved balance but not walking [23]. Task-specific training yielded superior results in the UL studies, but not in the gait studies.

As expected, visual and auditory feedback were presented by all of the systems with the visual presentation in either 2D or 3D. Most UL systems (six out of eight) were in 3D, whereas both gait studies were in 2D. The effect of the type of visual stimuli presentation in virtual rehabilitation is frequently discussed in a steadily growing literature. The majority of these studies compare UL activities performed in VEs with similar activities performed in real world environments [30], or compare immersive (3D) systems to flat-screen 2D systems [31, 32]. These two lines of inquiry identify differences in the kinematics of virtual UL and real world activities and differences in the kinematics of immersive and non-immersive virtual UL activities. Subramanian et al. [18•] identified differences reaching strategies developed in response to real world and virtual UE interventions. However, while the fidelity of movement is enhanced with 3D immersive systems, they are not superior to 2D non-immersive systems in promoting real world activity level motor outcomes.

Descriptions of *feedback* (KP and KR) were highly variable. There was great detail and attention to it in some papers [18•, 20•], reference to previous publications [15••, 16, 21••], and no specific mention in others [17, 19, 22]. Augmented feedback using KR was the predominant form of feedback provided in the UL studies. Exceptions to this were KP information on hand aperture [19] and trunk substitutions [18•]. Feedback also was distorted [20•] by providing error augmentation for arm trajectories. For the gait studies, feedback either was either not well described [23] or combined both KP (force generation and movement excursion of the foot) and KR [24•]. In the articles reviewed in this paper, there was no experimental manipulation of feedback making it difficult to determine whether combining KP and KR is superior to the provision of KR alone.

The *frequency, duration and distribution* of training in VR differed in some respects for the UL and gait studies. For both the UL and gait studies, training was typically distributed over a week. The duration on average tended to be approximately 4 weeks, but was 12 weeks for some UL studies. Total training time also was longer for the UL studies, with an average of 10.5 h of training compared to 7.5 h in the gait studies. For both the UL and gait studies, the differences in training time can be partially explained by greater time required for the systems that integrated robotics with VR. In addition, the gait study that required longer training duration (720 min) was performed in sitting [23], compared to the shorter training period performed in standing (270 min) [22].

Relationships between training dose and improvements in motor function emerged. UL studies supported a dose–response relationship between increased training dose and larger improvements in motor function identified by previous authors [31]. This trend was similar to the LL/gait studies, in which a larger dose of lower limb movements produced better outcomes [26] than a smaller volume of VR enhanced gait training [25].

Some of the strongest evidence related to the effectiveness of non-technology-based rehabilitation interventions suggests that outcomes are related to the dose of the intervention [32–35]. Training dose can be quantified as total treatment time or repetitions performed. This review only identified a single study in which training time was manipulated [19] experimentally, with better outcomes demonstrated by the group that trained in VR for a longer period of time. A large majority of the UL studies reviewed used a training time below the 16 h threshold dose associated with positive behavioral outcomes in the literature on non-automated rehabilitation of the upper extremity in

persons with sub-acute stroke [35]. It is not clear if training doses in VR will compare to real world training doses.

The number of repetitions performed during training is another important element of training dose. Only one UL [18•] and one gait study [24•] controlled for the number of repetitions performed by the two treatment groups. When controlling for repetitions in the UL study, there were no differences between groups with respect to impairment and activity-level motor outcomes. By contrast, in the gait study, while repetitions were comparable between groups, training duration was greater for the VR group compared to the non-VR group. The authors speculated that the cognitive requirements to complete the same number of movements in VR accounted for the increased duration of training [24•]. These findings raise the question of which dose parameters (duration and or repetitions) should be controlled for to allow dose-matched comparisons between real world and VR training.

Treatment *progression* was achieved with software algorithms and clinician-tester input. More UL studies (5 out of 8) used an algorithm for progression. For UL studies in the absence of an algorithm, treatment progression was not well described. Output parameters included assistance provided by the algorithm [19, 22] and movement error augmentation [19]. The most sophisticated algorithm used movement parameters such as smoothness of sub-movements to shape the motor behavior and progress the therapy [15••, 21••]. For gait studies, progression of treatment either was not reported [23] or based upon performance accuracy and tester observation [24•]. It appears that robotic interfaces have the advantage of using sophisticated algorithms for treatment customization and progression. Whether this benefit merits the cost is still not clear.

Outcomes of VR training were identified at all levels of the ICF continuum with a predominance of body-structure and activity measures. Several of the UL studies demonstrated statistically significant improvements at the body function level [15••, 17] and/or activity level [15••, 22] for both VR groups and dose-matched controls. None of these studies that compared group outcomes demonstrated significant time–group interactions. It is also interesting to note that the largest magnitude improvements were reported by the study that examined subjects in the acute stage of recovery [21••], while the smallest magnitude changes were reported for the study with the smallest total treatment dose. Beyond this clear observation, patterns for dose–response or acuity levels impacting outcomes were not apparent. Only one study demonstrated statistically significant improvements in a participation level measure [17]. This study utilized the MAL, a self-report comprehensive UL measure. Other articles not identifying statistically significant improvements, considered the Barthel Index, a global measure of ADL function [21••] and the SIS hand sub-scale a measure examining finger based activities [19].

For both gait studies, there was a transfer of training to either or both body structure and activity measures. The VR training using a treadmill was not superior to real world training for walking, but did improve balance [23]. By contrast, the robotic-interfaced training in sitting coupled with VR [24•] was significantly better than the robot-alone condition for both body function measures, such as kinetics at push-off and activity measures such as walking velocity. For the two studies included in this review, there was no standardization of measures, such as the walking velocity and endurance, across studies, making comparison of outcomes difficult. This is in part explained because both studies aimed to elucidate some of the biomechanical explanations for changes in motor behavior, rather than measure the activity of walking.

Conclusion

While the quantity of RCT's examining VR for stroke rehabilitation is growing, there remain unresolved questions about the technology, clinical characteristics, and practical concerns that will affect translation of VR rehabilitation into practice. We summarize them here in an effort to frame relevant questions for the field.

Unresolved questions related to the technology:

- Is it necessary to utilize haptic interfaces to provide tactile feedback and interactive forces, or we can achieve similar transfer of training by using mixed reality systems?
- Are semi-immersive 2D systems as efficacious as immersive systems in reducing impairments and promoting activity? Does the use of non-immersive systems promote compensations?
- Do software-controlled algorithms provide greater speed and fidelity of exercise progression? Are they superior to expert clinical decision-making? Can they be combined with clinician-decision making?

Clinical application questions related to participant selection and specificity of training:

- What are the minimal cognitive and perceptual requirements identified by standardized assessments to use virtual environments for sensorimotor rehabilitation effectively?
- How will differences in motor severity, chronicity, and type of task interact with VR system capabilities and dose requirements?

Practical considerations

- Will the cost of the sophisticated technology (such a robots interfaced with the VE's) justify the benefits?

We suggest that future studies should address both the efficacy of virtual rehabilitation interventions relative to the current standard of care, as well as comparing the efficacy and effectiveness of various approaches to presenting and delivering virtual interventions. In addition, while not the focus of this paper, studies that clarify the mechanisms underlying VR to stroke rehabilitation will complete our wish list. Comparative efficacy studies will enable us to answer the clinical and practical concerns, and the within-VR and mechanistic studies will aid in refining technology refinement, as well as elucidating the active ingredients in VR that will serve as a basis for stroke recovery.

Disclosure Dr. Deutsch is an inventor of virtual reality augmented systems. She presents CME on the topic of VR and Stroke.

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