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Use of Virtual Reality Cognitive Training to Improve Executive and Complex Attentional Functions: Can Virtual Reality Performance Predict Neurorehabilitation Outcomes?

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Abstract

Background: VR has proven successful in simulating activities and settings that prove inaccessible or unsafe to rehabilitate patients in. Current VR rehabilitation studies largely focus on assessing cognitive skills, not on training cognitive deficits. The current study focused on repeated exposure with a VR-based cognitive intervention to improve deficits known to impact the ability to resume complex activities. Associations between the VR Stroop and neuropsychological, speech therapy, and global rehabilitation measures were examined. We included a brain injured control group to address this frequently cited methodological concern.

Design: This was a mixed design study with quasi-experimental Intervention group (N = 12) and retrospective Control group (N = 12). Both groups comprised individuals with brain injury admitted to an outpatient day neurorehabilitation program.

Results: Patients with higher level of education and shorter acute medical course deliberated longer before responding on specific Virtual Stroop indices. The brain injury group receiving Virtual Stroop intervention demonstrated a significant increase in level of independence in the home and in community participation by discharge from day neurorehabilitation, compared with the Control group. Increased independence of the virtual reality group was associated with improved attention and self-monitoring, and less disinhibition on the Virtual Stroop.

Conclusion: Patients with brain injury demonstrated improvements in various executive functioning and attention indices on the Virtual Stroop, compared with patients who received standard neurorehabilitation. Neurocognitive training within an immersive real-world setting was associated with improved global and specific neurorehabilitation outcomes. Performance on the Virtual Stroop also demonstrated a relationship with cognitive flexibility on traditional neuropsychological testing.

Keywords: Brain Injuries; Virtual Reality Exposure Therapy; Executive Function; Rehabilitation

Introduction

Virtual reality (VR) is an emerging technology with potential benefits in the realms of rehabilitation assessment, treatment, and research. VR enables presentation of ecologically valid stimulus environments that reflect the challenges of everyday life that tax executive functions [1-4]. However, executive demands are being elicited in a relatively safe environment. Executive functions are cognitive processes that allow humans to select, control, and monitor their behaviors. They include inhibition of impulses, mental manipulation of information, reasoning, planning, problem-solving, and executive control in the form of complex attentional processes, such as vigilance, sustained attention, selective attention, and shifting and dividing attention among multiple tasks simultaneously [5-8]. Degree of congruence between VR and real-world environments is important given that one of the criticisms of current executive functioning measures and rehabilitation care is that even evidence-based interventions do not consistently generalize to patients' home, school, or work settings [9-11]. In addition to enhanced generalizability, VR studies have demonstrated that patients/subjects are more motivated in virtual environments than conventional settings [3,12-15]. VR has proven successful in simulating and training in various settings, including education, military operations, operation of vehicles and airplanes, and in medicine [16-18]. Although initial applications of VR in specific medicine and psychology specialties have demonstrated promise, little is yet known about how to effectively integrate VR into the rehabilitation realm.

Virtual Reality and Rehabilitation

Traumatic brain injury and stroke

VR rehabilitation studies are few in number and have predominantly focused upon assessing cognitive skills and real-world performance [19]. Jovanovski et al. [20] examined the ability of 13 individuals with moderate or severe traumatic brain injury (TBI) or stroke to complete errands under time constraints, using the Multitasking in the City Test (MCT). The MCT included landmarks such as a post office, grocery store, and coffee shop. Patients kept track of items in their backpack and the amount of money in their wallet [20]. Those with ABI took nearly twice as long to complete tasks, committed errors more frequently, and failed to meet deadlines compared with Controls. They also spent nearly twice as long planning than Controls. The additional time taken by patients with ABI is in contrast to findings observed for the Multiple Errands Test (MET), in which ABI patients initiated the

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test without developing a plan [21]. The MET is executed in a real-life (not VR) setting. Measures of cognitive flexibility, inhibition, and problem-solving were correlated with MCT completion time and total errors [20].

Raspelli et al. [7] developed a VR-based version of the MET, to assess efficiency in sequencing of specified shopping tasks, completion time, and rule break errors in stroke patients, using a virtual supermarket setting. Individuals post-stroke broke more rules and were less efficient in completing tasks on the VR-based MET, discriminating individuals following stroke from healthy individuals. They took less time to complete tasks than healthy individuals. The VR-based MET was found to be highly correlated with traditional neuropsychological measures assessing attentional set-shifting, response inhibition, interference, and cognitive flexibility [7,22,23].

In a study using the Virtual Action Planning-Supermarket (VAP-S), participants were asked to purchase grocery items from a list and then pay for them at a cash register [24]. Patients post-stroke acquired grocery items with the fewest steps compared with a mild cognitive impairment (MCI) and a schizophrenia group. Patients post-stroke remembered to purchase a greater number of grocery items, but were as slow as and made more incorrect actions than a group with schizophrenia [24]. In another VR grocery store study, patients with stroke asked to purchase items based on description and price committed significantly more attentional, memory, and executive-based errors and they took longer to complete tasks than healthy controls [25].

Patients with TBI who completed office-based tasks in a virtual office (Assessim Office), exhibited greater working memory difficulties, tending to refer to manualized instructions more than patients with multiple sclerosis (MS) [26]. Both groups demonstrated significantly more problem-solving difficulties than healthy controls [26].

In a study focused on skill development, patients with TBI who received 10 45-min VR-based treatment sessions in a VR supermarket (VMall) demonstrated stronger ability to complete a multiple errands protocol and activities of daily living in vivo compared with those who received 10 sessions of conventional occupational therapy. Between and within group differences were not significant [27].

Brain Neoplasm

Thirty-eight medically stable patients diagnosed with brain tumor were randomized to either VR treatment or a Control condition [15]. In the VR condition, patients participated in increasingly physically demanding tasks by using their paretic/plegic upper extremity to move, punch, or stop virtual objects surrounding their image on a computer screen (3 times/week), and their weekly regimen was supplemented by computer-assisted cognitive rehabilitation (CCR), supplying training in attention and memory (2 times/week). The Control group only received CCR [15]. Patients receiving VR training demonstrated significant improvements in sustained attention, vigilance, and working memory, as well as visuomotor attention and processing speed [15]. More treatment studies targeting executive abilities in an effort to improve real-world functioning are necessary.

This study explores the possibility of improving real world functioning in brain injury survivors by integrating VR-based treatment of specific executive (cognitive flexibility, inhibition) and complex attention functions (sustained attention, selective attention) into an outpatient neurorehabilitation milieu. It was hypothesized that patients would evidence stronger complex attention, inhibition, and processing speed, upon conclusion of treatment using the VR Stroop. Outcomes of patients with brain injury receiving VR treatment were compared to those receiving traditional neurorehabilitation interventions. Patients receiving VR intervention were expected to demonstrate stronger neuropsychological and speech therapy performance, and receive better ratings on global rehabilitation outcome measures, in comparison with a demographically-matched control group.

Methods

Procedure

Participants were persons with acquired brain injury (ABI) and resultant dysfunction in executive and attention skills, currently enrolled in an outpatient multidisciplinary neurorehabilitation program (Day Neuro). There were 69 consecutive admissions into the Day Neuro program from 08/2014 to 05/2015. Data were obtained from 21/69 patients meeting inclusion criteria (Figure 1). There was no random allocation. A demographically-matched historical Control

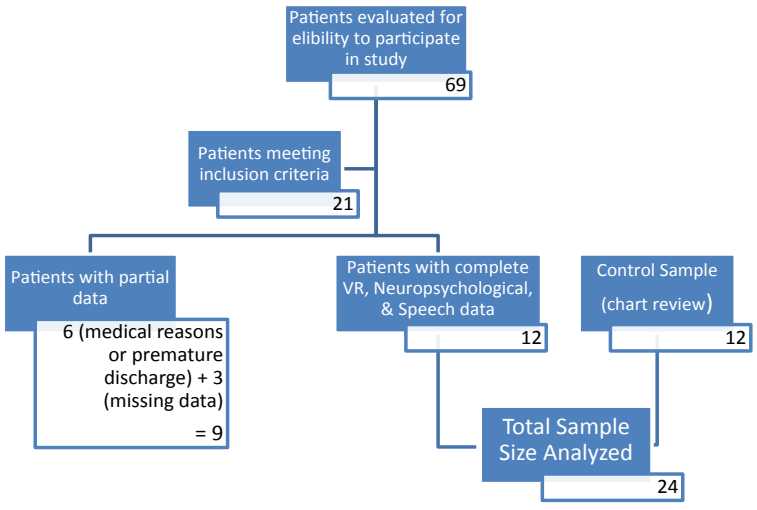

Figure 1: Final sample size analyzed.

group was included (n=12).

The outpatient program is part of the continuum of care that includes a trauma center, inpatient rehabilitation facility, and comprehensive outpatient program. Day Neuro is a weekday program (9AM-3PM) that includes traditional rehabilitation care such as physical, occupational, recreation, and speech therapy, as well as non-traditional services such as driving instruction, aquatics therapy, and home-based care. Individuals participated in Day Neuro once discharged from inpatient rehabilitation. Timing of neuropsychological evaluations varied, but typically occurred within 1-2 weeks prior to discharge from the Day Neuro program.

Approval to complete the study was obtained from the hospital's institutional review board and it was conducted in accordance with the Declaration of the World Medical Association. All patients meeting inclusion and exclusion criteria of the study completed informed consent to participate. The ClinicalTrials.gov Identifier for this study is NCT04017091.

Inclusion criteria

Patients participating in this study were aged 18 years and older, diagnosed with acquired traumatic or non-traumatic neurologic illness, and with dysfunction in executive and attention skills documented during their inpatient rehabilitation course.

Patients that had not yet undergone a neuropsychological evaluation by the time they consented to participate in the study, were administered the Orientation and Cognitive Log (OLOG/Cog-Log) to ensure they were oriented and had sufficient cognitive ability to attend to and understand instructions.

Exclusion criteria

Patients were excluded from participating if they were medically unstable, as deemed by their primary doctor; aphasic or had hemispatial neglect; had prior history of significant neurological complications or developmental delay resulting in compromised cognition, prisoners, and if they did not speak English.

Participants

ABI patients

Twenty-one patients with ABI participated in this pilot study Figure 1: 9 diagnosed with stroke (43%), 6 with TBI (29%), 2 with anoxic injury (10%), 3 with brain tumor (14%), and 1 with amyloid angiopathy (5%). Six of the 21 patients partially completed the study, but failed to complete all 8 intervention sessions: Two patients were medically withdrawn from Day Neuro due to refractory medical complications, two patients self-discharged from the program against medical advice, and two patients' rehabilitation regimens were concluded prior to their projected discharge dates when insurance or state-assisted benefits were not extended. Of the remaining 15 participants, 12 completed neuropsychological evaluation. The final analyses included 12 patients with ABI who completed VR treatment and all neuropsychological and rehabilitation outcome measures, and 12 Controls with ABI (Figure 1).

The 12 ABI patients comprising the VR group were a mean of 37 years of age, 75% were male, and half of the group was Caucasian. Ninety-one percent of the group had at least a high school degree, 75% were living independently, and 75% were employed prior to their injury/condition. The duration of VR patients' acute medical stay ranged from about 9-20 days, their inpatient rehabilitation stay ranged from 14-34 days, and their outpatient day neurorehabilitation stay ranged from 23-79 days.

Control group

The 12 Controls were age- and gender-matched (and etiology when possible) patients who had previously received traditional neurorehabilitation and completed the same measures as the VR group prior to onset of the study, but they did not receive VR treatment. There were no significant differences in demographic or clinical variables between the VR and Control groups.

The 12 Control patients were a mean of 36 years of age, 67% were male, and half of the group was Caucasian. Eighty-five percent of the group had at least a high school degree, 83% were living independently, and 75% were employed prior to their injury/condition. The duration of these patients' acute medical stay ranged from about 10-17 days, their inpatient rehabilitation stay ranged from 14-30 days, and their outpatient day neurorehabilitation stay ranged from 12-42 days.

The Control group's data was obtained via retrospective chart review of patients admitted to Day Neuro between 04/2013 and 07/2014.

Intervention Schedule

Patients completed the VR apartment program twice per week for a 4-week period (8 session's total). The VR interventions replaced 60-90 minutes of speech therapy and/or 60-90 minutes of independent time (time designated for relaxation or completion of therapy assignments) per week of the study. Otherwise, clinical services were not altered (Appendix 1 for detailed schedule of VR and Day Neuro therapy regimen).

The total duration of sessions 1 and 8 was approximately 60 minutes each. The duration of sessions 2-7 was 30 minutes each.

Intervention Measures

Bimodal VR-Stroop (ClinicaVR: Apartment Stroop)

Within this VR apartment, patients were seated in a living room, in front of a flat-screen TV, a kitchen, and a window (Figure 2). This intervention consisted of two Stroop conditions across all 8 sessions. In Condition 1 (Inhibition), a series of color rectangles appeared on the television screen (blue, red or green) while the name of one of these colors was verbally recited through the computer speakers by a female voice at the same pace (bimodal presentations). Clicking a mouse with the preferred hand as quickly as possible indicated when the color named (audio stimulus) matched the color shown (visual stimulus). Participants were to withhold their response in mismatched trials. A total of 144 stimuli were presented, including 72 targets [28]. During the task, 14 distracters appeared in different areas of the environment (center, left, or right). Some distracters were audio–visual (School Bus passing on the street, Toy Robot on the floor), others were auditory (Doorbell, Vacuum Cleaner), and some were visual (Paper plane, Woman Walking in Kitchen). Distracters were displayed for 5 seconds, and presented in equally appearing intervals of 10, 15, or 25 seconds.

Session 1 (baseline) included all types of distracters (auditory, visual, audio–visual) simultaneously. Sessions 2 and 3 included no distracting stimuli. To gauge whether the presence of distracters increased executive burden, distracters were then reintroduced at session 4, varying them by sensory modality. Specifically, sessions 4 and 5 included only auditory distracters, and sessions 6 and 7 included only visual distracters. Session 8 resembled baseline by including all types of distracters again, to gauge change in performance between sessions 1 and 8.

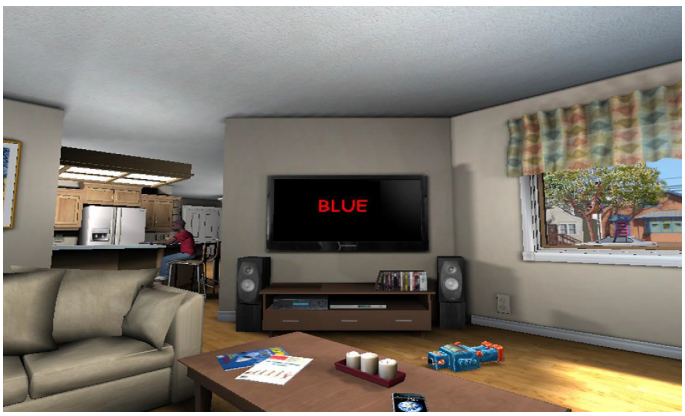

Figure 2: ClinicaVR: Apartment Stroop

In Condition 2 (Interference), color words were presented on the screen, written with matched ink color (Congruent Trial: e.g. BLUE written in blue) or different ink color (Incongruent Trial: e.g. BLUE written in red). Participants clicked the mouse when the color heard was the same as the ink color; not the word printed. Again, a total of 144 stimuli were presented, including 72 targets, divided into 36 congruent and 36 incongruent stimuli. Distracters in Condition 2 were the same as those in Condition 1. Total task duration, including both conditions, was 9.6 minutes. Outcomes recorded included: (1) response times for correct and incongruent trials; (2) total commission errors; and (3) total omission errors.

Devices

Participants were fitted with a Z800 3DVisor head-mounted display (HMD) system. The HMD was used to create a 3D-like effect allowing patients to look 360 degrees around themselves by turning their head. This HMD system has been approved by the U.S. Food & Drug Administration as part of a therapeutic application and has previously been used in rehabilitation patients with balance disorders, vertigo, or instability by the medical hardware developer Medicaa. A laptop was placed central to the seated patient and responses to the VR and 2-dimensional computer measures were registered when the patient depressed the computer mouse.

Outcome Measures

Neuropsychological measures

(1) Wechsler Test of Adult Reading (WTAR) was used to determine patients' estimated premorbid intelligence quotient [29].

(2) Trail Making Tests (TMT) assessed visual attention, visuomotor processing speed, and cognitive flexibility [30,31].

(3) Verbal Fluency Tests (COWAT and Animals) assessed rapid word generation in response to phonemic and conceptual cues [32].

(4) Stroop Color and Word Test, Golden version assessed sustained attention and the ability to inhibit cognitive interference [33].

Speech therapy measures

Functional Assessment of Verbal Reasoning and Executive Strategies (FAVRES) [34]. Performance on the Make a Decision subtest (deciding on a gift) was examined in this study. Accuracy Raw and Analysis of Reasoning Raw scores were the variables of interest. In addition, (1) Problem Solving and (2) Organization subtests of the Ross Information Processing Assessment (RIPA), 2nd Edition were used [35].

Global rehabilitation outcome measures

The Holistic Outcome Measure (HOM) is a 3-item measure developed by a speech-language pathologist at the rehabilitation institute in which this study was conducted (unpublished) and is used throughout the Day Neuro course to evaluate patients' level of independence in (1) the home, (2) the community, and (3) community participation (Appendix 2). Ratings are made on a 5-point scale where 1 indicates a need for full-time supervision and participation is limited to medical appointments, and 5 indicate full independence. Subscale and total HOM scores were examined at admission to and discharge from Day Neuro.

Mayo-Portland Adaptability Inventory, 4th Edition (MPAI-4) [36]. The MPAI-4 consists of three subscales designed to evaluate sensory, cognitive, and motor abilities (Ability Index), emotional and neurological symptoms, interpersonal adjustment, and awareness (Adjustment Index), and social, work, and leisure participation and management of IADLs (Participation Index) in individuals with ABI [36]. Items are ranked from 0 to 4 with lower scores indicating greater independence. Subscale and total scores were examined at admission to and discharge from Day Neuro. This study analyzed scores provided by patients and clinicians only.

Symptom self-report questionnaire

The Simulator Sickness Questionnaire (SSQ) was completed by patients upon conclusion of sessions 2 through 7 to assess the occurrence, nature and severity of sickness symptoms induced by VR environments. The SSQ comprises 16 items rated on a scale from 0 to 3 (0=no symptom; 1=slight; 2=moderate; 3=severe) [37].

Based upon prior research, multiple patient demographics and clinical factors that may influence functional outcomes were included in analyses conducted in this study. These included age, sex, race/ethnicity, marital status, years of education, employment, independence level at discharge, and length of medical and rehabilitation stay [38,39].

Statistical Analysis

All analyses were conducted using SAS, version 9.4 (SAS Institute Inc., Cary, North Carolina). Two-tailed p-values ≤ 0.05 were considered

statistically significant. Descriptive statistics were summarized as means and standard deviations or medians and interquartile ranges for continuous variables. Percentages and frequencies were used for categorical variables. Comparisons between the Study group and Control group were made using a Student's t-test or a Wilcoxon-Mann-Whitney test for continuous variables, and Fisher's exact test for categorical variables. Pearson correlations were used to summarize the relationship between neuropsychological outcomes and the change in performance from Session 1 to 8 on VR conditions. The relationship between change in VR performance and change in scores on both rehabilitation outcome measures from admission to discharge was also examined. Between-group comparisons on the HOM and MPAI-4 were examined.

Results

Table 1 summarizes patient demographics and length of medical, inpatient rehabilitation, and day neurorehabilitation stays (LOS). There were no significant differences between the VR and the Control group.

Associations Between VR Variables and Demographic and Clinical Variables.

Education demonstrated a relationship with change in performance from Session 1 to 8 on the VR apartment. Better educated individuals with ABI and those with shorter acute medical courses deliberated longer before providing correct responses on the color-naming condition (Table 2).

VR and Neuropsychological Outcomes

The VR and Control group were compared on specific paper-and-pencil neuropsychological measures. Performance on an estimate of premorbid intellectual functioning (WTAR) was statistically significantly different. The Control group had relatively more modest WTAR scores (Standard Score: 84 (75-94); low average range), in comparison with average range performance for the VR group (Standard Score: 96 (92-110), $p = 0.011$). Poorer performance on Trial Making Test: Part B, assessing cognitive flexibility and visuomotor processing speed, was significantly and modestly correlated with longer time to give a correct response on the VR apartment interference condition ($r=0.59$, $p<0.05$).

	All (n=24)	VR Group (n=12)	Controls (n=12)	p-value
Age, mean (sd)	35.8 (16.0)	36.8 (4.9)	35.7 (4.9)	0.885
Gender				0.653
Male	17 (71%)	9 (75%)	8 (67%)	
Female	7 (29%)	3 (25%)	4 (33%)	
Ethnicity/Race				0.842
Black	7 (29%)	3 (25%)	4 (33%)	
Hispanic	5 (21%)	3 (25%)	2 (17%)	
White	12 (50%)	6 (50%)	6 (50%)	
Years of Education				0.642
<12	3 (12.5%)	1 (9.1%)	2 (15.4%)	
12-16	21 (87.5%)	10 (90.9%)	11 (84.6%)	
16+	0 (0%)	0 (0%)	0 (0%)	
Diagnosis				0.519
Stroke	9 (37.5%)	5 (42%)	4 (33%)	
TBI	11 (46%)	4 (33%)	7 (58%)	
Tumor	3 (12.5%)	2 (17%)	1 (8%)	
Anoxia BI	1 (4%)	1 (8%)	0 (0%)	
Living Independently				0.591
Yes	19 (79%)	9 (75%)	10 (83%)	
With Parents	4 (17%)	2 (17%)	2 (17%)	
With Caretaker	1 (4%)	1 (8%)	0 (0%)	
Employment				0.590
Employed	18 (75%)	9 (75%)	9 (75%)	
Student	3 (12.5%)	2 (17%)	1 (8%)	
Retired	2 (8%)	0 (0%)	2 (17%)	
Not Employed	1 (4%)	1 (8%)	0 (0%)	
Time Variables				
Medical LOS (days), median (IQR)	11 (7.5-20)	11 (8.5-20)	9.5 (6-17)	0.487
Rehab LOS (days), median (IQR)	19 (14-31.5)	19.5 (13.5-33.5)	19 (14-29.5)	0.772
Day Neuro (days), median (IQR)	35 (13.5-67)	49.5 (22.5-79)	20 (11.5-42)	0.126

BI=Brain Injury, IQR=Interquartile Range, SD=Standard Deviation, TBI=Traumatic Brain Injury, VR=Virtual Reality

Table 1: Demographic and clinical information of virtual reality group and control group.

	Age[a]	Education[b]	Medical LOS[a]	Rehab LOS[a]
Color Naming				
Total number of correct responses	-0.415	0.198	0.099	-0.058
Average response time for correct responses	-0.319	0.208	-0.375	-0.048
Shortest response time for correct responses	-0.242	0.182	-0.293	0.007
Longest response time for correct responses	-0.116	**0.604**[*]	**-0.660**[*]	-0.479
Total number of incorrect responses	-0.309	0.012	-0.284	0.000
Average response time for incorrect responses	-0.415	0.000	-0.340	-0.211
Longest response time for an incorrect response	-0.265	-0.049	-0.326	-0.296
Stimuli that were correct unanswered	0.294	-0.125	0.323	-0.062
Total number of omissions	0.415	-0.198	-0.099	0.058
Word Reading				
Total number of correct responses	-0.475	0.136	-0.125	-0.202
Average response time for correct responses	-0.418	-0.179	0.016	0.102
Shortest response time for correct responses	0.400	-0.336	-0.153	-0.008
Longest response time for correct responses	-0.156	-0.046	0.048	-0.334
Total number of correct responses for congruent stimuli	0.404	-0.152	0.206	0.100
Mean response time for congruent stimuli	-0.311	-0.293	0.107	0.041
Shortest response time for congruent stimuli	0.340	-0.444	-0.112	0.026
Longest response time for congruent stimuli	-0.247	-0.174	0.204	-0.104
Interference				
Total number of correct responses to incongruent stimuli	-0.501	0.214	-0.139	-0.208
Average response time for incongruent stimuli	0.306	-0.091	0.084	-0.236
Shortest response time for incongruent stimuli	0.469	-0.100	0.172	-0.219
Longest response time for incongruent stimuli	-0.046	-0.228	-0.012	-0.352
Total number of incorrect responses	-0.104	-0.197	-0.158	-0.150
Average response time for incorrect responses	-0.350	-0.444	-0.082	0.267
Shortest response time for an incorrect response	-0.402	-0.350	-0.063	0.325
Longest response time for an incorrect response	-0.231	-0.228	-0.104	0.200
Stimuli that were correct unanswered	0.033	0.217	0.131	0.172
Total number of omissions	0.470	-0.153	0.118	0.209

[a]Pearson correlation, [b]Spearman correlation, [*]Significant at 0.05, [†]Significant at 0.01

Table 2: Correlations between demographics and length of stay (LOS) variables vs change in performance on variables of the virtual reality apartment conditions: color naming, word reading, and interference.

	VR Group		Control Group		
	N	Median (IQR)[*]	N	Median (IQR)[*]	
Admit					
HOM Supervision Home	12	1.5 (1,2)	12	3.5 (1.5,4.5)	**0.019**
HOM Supervision Community	12	2 (1.5,2)	12	2 (1,4)	0.644
HOM Community Participation	12	2 (2,2)	12	3 (2,4)	**0.002**
HOM Total Score	12	5.5 (4.5,6)	12	8 (5.5,12.5)	**0.024**
Discharge					
HOM Supervision Home	12	4 (3,5)	12	5 (3,5)	0.278
HOM Supervision Community	12	3.5 (3,4)	12	4 (3,4)	0.602
HOM Community Participation	12	3 (3,4)	12	4 (3,4)	0.126
HOM Total Score	12	11 (9,12.5)	12	12.5 (9.5,13.5)	0.221
Difference					
HOM Supervision Home	12	2 (1,3)	12	1 (0,1.5)	**0.030**
HOM Supervision Community	12	1 (1,3)	12	1 (0,2)	0.455
HOM Community Participation	12	1 (1,2)	12	1 (0,1)	**0.014**
HOM Total Score	12	4.5 (3,8)	12	2.5 (1,4.5)	**0.047**

[*]IQR – Interquartile range, Holistic Outcome Measure (HOM)

Table 3: Differences in supervision needs and participation level between the virtual reality and control groups on Holistic Outcome Measure (HOM) following virtual reality intervention.

VR and Neurorehabilitation Outcomes

There were no significant group differences for speech therapy variables.

On the measure of global improvement in level of independence (HOM), participants in the Control group were significantly more independent in the home and engaged in community participation at the time of admission to Day Neuro (Table 3). However, those in

	HOM Change Score (Discharge - Admit)			
Virtual Reality Apartment Stroop Variables (Session 8 – 1)	**Supervision Home**	**Supervision Community**	**Community Participation**	**Total**
Color Naming				
Total number of correct responses	0.519	**0.659***	0.297	**0.611***
Average response time for correct responses	-0.160	-0.410	0.099	-0.245
Total number of incorrect responses	0.170	0.388	0.175	0.293
Average response time for incorrect responses	-0.230	-0.029	0.292	-0.070
Total number of omissions	-0.519	**-0.659***	-0.297	**-0.611***
Word Reading				
Total number of correct responses	0.433	0.514	0.554	0.552
Average response time for correct responses	-0.312	-0.412	0.148	-0.312
Shortest response time for correct responses	-0.371	-0.232	-0.311	-0.347
Longest response time for correct responses	0.056	0.131	0.476	0.178
Interference				
Total number of correct responses	0.430	0.524	**0.578***	0.559
Average response time for correct responses	-0.254	-0.048	0.004	-0.146
Total number of incorrect responses	-0.342	-0.320	0.246	-0.266
Average response time for incorrect responses	-0.159	-0.190	-0.083	-0.180
Total number of omissions	-0.432	-0.514	-0.561	-0.552
*Significant at 0.05, Holistic Outcome Measure (HOM)				

Table 4: Correlations between difference score of virtual reality apartment Stroop and difference score of Holistic Outcome Measure (HOM).

	Virtual Reality Patients n (%)
Simulator Sickness Questionnaire Item #	
SSQ 1 – General Discomfort	3 (20%)
SSQ 2 – Fatigue	6 (40%)
SSQ 3 - Headache	1 (6.7%)
SSQ 4 – Eyestrain	4 (26.7%)
SSQ 5 – Difficulty Focusing	4 (26.7%)
SSQ 6 – Salivation Increasing	0 (0%)
SSQ 7 – Sweating	1 (6.7%)
SSQ 8 – Nausea	0 (0%)
SSQ 9 – Difficulty Concentrating	4 (26.7%)
SSQ 10 – Fullness of the Head	0 (0%)
SSQ 11 – Blurred Vision	3 (20%)
SSQ 12 – Dizziness with Eyes Open	1 (6.7%)
SSQ 13 – Dizziness with Eyes Closed	0 (0%)
SSQ 14 – Vertigo	1 (6.7%)
SSQ 15 – Stomach Awareness	0 (0%)
SSQ 16 – Burping	0 (0%)

Table 5: Simulator Sickness Questionnaire (SSQ) endorsements during sessions 2 through 7.

the VR group made significantly greater improvements in home independence and level of community participation by discharge. There were no significant differences between these two groups on the MPAI-4. Improvement in accuracy (number correct) and fewer omission errors on color-naming trials of VR apartment stroop (session 8-1) was significantly associated with greater independence in the community and higher global outcome scores on the HOM (discharge-admission). Improvement in accuracy on interference trials of VR apartment stroop was significantly associated with greater social/leisure participation by discharge (Table 4). This indicated that stronger ability to inhibit an automatic response was associated with greater participation. Overall reduced response time was also associated with increased independence for the VR group by discharge, though reaction time indices did not reach significance.

Ten of the 16 items were positively endorsed by patients on the SSQ across sessions (Table 5). General discomfort (n = 3; 20%), fatigue (n = 6; 40%), eye strain (n = 4; 26.7%), difficulty focusing or concentrating (n = 4; 26.7%), and blurred vision of mild or moderate degree (n = 3; 20%) were most consistently endorsed by patients across sessions on the SSQ. By the fourth session, the number of patients reporting HMD-related symptoms declined to four. No adverse events occurred and no patients volitionally withdrew from the study.

Discussion

To date, use of VR in neurorehabilitation is not systematic and studies supporting use of VR as a therapeutic treatment in medical rehabilitation remains limited. This study sought to compare outcomes of patients with ABI receiving VR treatment with those

receiving traditional neurorehabilitation only. Given that absence of a Control group is noted to be a limitation in multiple VR studies, patients with ABI matched on age, gender, and etiology were included [12]. This study revealed that patients who completed VR treatment demonstrated greater home independence and community participation by discharge from rehabilitation compared with the Control group. Improved accuracy and fewer omission errors on the VR apartment Stroop was associated with these areas of increased independence. Stated differently, improved attention and executive self-monitoring and inhibition in the VR group were associated with increased independence. These associations were found on the HOM, which assesses independence in managing more routine IADLs and participation in leisure, but not on the MPAI-4 which assesses higher-level IADLs.

ABI patients were more likely to respond impulsively in the VR Stroop interference condition compared with non-VR Stroop measures in a similar study by this group [40]. The VR version of the Stroop is sensitive in capturing dysexecutive deficits in neurological patients, but practice in the VR environment can reduce these deficits.

Regarding predictors, higher education and shorter acute medical course were associated with longer deliberation time during the VR stroop color-naming condition.

In accordance with the literature, specific VR indices demonstrated associations with a measure assessing divided attention [26]. Poorer performance on Trial Making Test: Part B was associated with slower response time on the interference condition of the VR apartment stroop. No relationship was found with relatively more simple attention, inhibition, and processing speed paper-and-pencil measures. The absence of associations with 2-dimensional neuropsychological and speech therapy measures raises the question about whether VR-based interventions and traditional measures quantify cognitive and neurobehavioral output in the same way. Some researchers criticize current evidence-based executive functioning interventions for not consistently generalizing to real-world environments [9-11].

The lack of association between speech therapy executive variables and VR indices may be attributable to the fact that FAVRES scoring levels were not granular enough to capture between-group differences. Patients participating in this study needed to comprehend instructions and verbalize questions. Patients meeting inclusion criteria for this study may have had relatively stronger language and executive skills, precluding differentiation between VR and Control groups on the RIPA battery.

These findings have important implications for the treatment of executive functions in patients with ABI. Repeated practice of executive tasks while "virtually" exposed to distractions typically encountered in an apartment/home setting was associated with improved attention, self-monitoring, and inhibition for patients with ABI. More importantly, these improvements were associated with increased home independence and community participation – important goals to patients, their families, and rehabilitation clinicians. Inclusion of a processing speed component is important, to potentially identify those with more severe deficits and enable patients to perform executive functions in real time. These are important considerations for developers of VR technology intended to train and rehabilitate patients, in order to further enhance ecological validity.

Study Limitations

Due to small sample size, low power may have impacted detection of some group differences, and possibly associations between VR indices and neurorehabilitation outcome measures. However, it should be noted that most VR studies are comprised of fewer than 30 participants. The relatively small sample size prevented us from examining differences by severity and etiology. The study groups consisted of mixed neurological etiologies.

Though few participants reported symptoms associated with HMD use, it was possible that due to cognitive deficits their reports were confounded with their general condition associated with CNS injury, as opposed to reporting new onset symptoms associated with simulator sickness.

There were no associations between VR measures and speech therapy measures in this study. Other FAVRES subtests may have been more sensitive and related to executive functions comprising the VR treatments. Insufficient data of other FAVRES subtests was available for patients who completed all study measures, and therefore were not selected.

Data was based on clinician ratings for both the HOM and MPAI-4. Both measures consider a patient's cognitive and physical abilities, and the degree to which impairments in these domains impact level of functioning and participation. However, differences in their associations with the VR variables may be explained by the fact that the HOM considers independence in the home and community more broadly - a closer match to the VR environment used in this study. It does not evaluate an individual's emotional well-being and ability to manage more complex instrumental activities of daily living as the MPAI-4 does (e.g. driving and paying bills), which may explain the absence of associations between the MPAI-4 and VR variables in this study. Rehabilitation participation, degree of psychosocial support, types of specialty services offered (e.g. educational groups), and pre-existing illnesses were not analyzed in this study. Additional factors may explain findings from this study. Early in recovery, there is potential that improved outcomes may be due to natural recovery from illness, rather than the intervention introduced. This is less likely in the current study, given that patients were a mean of 13-14 weeks post injury, with patients typically discharging after 2 months of outpatient neurorehabilitation. Also, it is possible that improved outcomes were attributable to increased intensity of rehabilitation, given that the VR group received potentially 5 additional hours of therapy compared to the Control group. The Day Neurorehabilitation program is a relatively structured multidisciplinary outpatient program in a medical center-affiliated rehabilitation center. The findings from this group of patients may not necessarily generalize to other neurorehabilitation populations.

Conclusion

This study provided preliminary support that use of VR training in cognitive neurorehabilitation is associated with improvements in attention and executive functions, as evidenced by better accuracy, better self-monitoring, and less disinhibited responding in patients with ABI. Patients' performance in an immersive real-world (VR) apartment was associated with improvements in global and specific neurorehabilitation outcomes. This was true for lower-level IADLs. Additionally, there were no adverse events associated with use of VR in this neurological population. Replication of these findings on a larger sample and outcome measures measuring similar constructs is a necessary step before making VR an integral part of the neurorehabilitation regimen. Nonetheless, these findings support the ease with which VR cognitive interventions can be delivered in the neurorehabilitation milieu. This may increase delivery options of neurocognitive rehabilitation treatments in different settings: bedside inpatient or residential facilities, outpatient clinics, or patients' homes.

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Conflicts of Interest

There is no conflict of interest to report, as no financial benefit will be conferred on the authors as a result of the research supporting this article.

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Others

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