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Immersive Virtual Reality Training Improved Upper Extremity Function in Patients with Spinal Cord Injuries: A Case Series

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IMMERSIVE VIRTUAL REALITY TRAINING IMPROVED UPPER EXTREMITY FUNCTION IN PATIENTS WITH SPINAL CORD INJURIES: A CASE SERIES

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University of Nebraska Medical Center, 2020

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ABSTRACT:

Virtual reality (VR) is an emerging treatment tool to engage people in environments that appear and feel similar to real-world objects and events.[1] There are various levels of evidence that VR can potentially promote functional activity and neuroplasticity in patients with neurological disorders like spinal cord injury (SCI).[2,3] In this case series, we explored the feasibility of using commercially available immersive VR technology as an augmented treatment in the SCI population and compare participant's suitability for this intervention. Three male SCI participants were recruited in a subacute inpatient rehabilitation facility and participated in VR intervention twice a week in addition to their conventional therapies. Manual strength and functional testing were recorded biweekly until participants discharged. Training includes reaching activities, wrist rotation, gripping, and thumb movement to simulate real-life activities. A questionnaire regarding their experience with VR training was administered at the end. All participants had improvement in strength and functional tests. 9-hole peg test demonstrated clinically meaningful change in two of three participants. Manual muscle test changes were 2, 4.5

and 13.5 points individually. Participants with lower manual muscle test scores at baseline showed more potential to change compared to those who had high scores, which would possibly due to plateau effect. Pinch and grip strength demonstrated small changes which were not clinically important. Participants also rated VR technology of high reality level and great enjoyment in the questionnaire. This case series suggests that immersive VR with head mount display may be viable to provide safe and effective treatment for patients with SCI. VR training appears to be a possible adjunct to physical and occupational therapy as a method of muscle strengthening, improving upper extremity function and improving motivation during subacute rehabilitation.

KEYWORDS: Immersive Virtual reality, Spinal cord injury, Neuroplasticity, Oculus, Leap Motion

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LIST OF ABBREVIATION

ABI: acquired brain injury

ASD: autism spectrum disorders

CVA: cerebrovascular accident

L: left

MMSE: mini-mental status examination

MMT: manual muscle testing

MVA: motor vehicle accident

R: right

ROM: range of motion

SCI: spinal cord injury

Sec: second

UE: upper extremity

VR: virtual reality

Chapter One: Literature Review

Virtual reality application in healthcare field

As virtual reality (VR) technology is becoming more and more mature and popular on the market, it turns into a trend for health care systems to integrate VR in their education and health care technology landscape. A growing number of medical institutions across the world apply virtual reality to deliver health care education for students, staff, and patients. Additionally, an increasing number of health care institutions are providing actual care in virtual worlds. Even it sounds so familiar to us. The question is: What is exactly VR?

1. History and introduction to VR

The first healthcare applications of VR started in the early 90s due to the need for medical staff to visualize complex medical data, particularly during surgery and for surgery planning[4].

VR has been generally defined as "use of interactive simulations created with computer hardware and software to present users with opportunities to engage in environments that appear and feel similar to real-world objects and events".[5] More specifically, VR can be viewed as a tool to advance human-computer interaction. Computers can generate a virtual environment that responds to human interaction in a naturalistic and real-time fashion. Humans can control and modify the environment to achieve an effect that is hard to realize in the real world. VR can be created to assess and rehabilitate cognitive and motor functions, providing interactive scenarios designed to target client needs and preferences.

Interaction in the three dimensions is a key characteristic that distinguishes a VR experience from other robotic arm or gaming systems used in the rehabilitation field. For example, users could walk and turn around to explore a virtual landscape or inspect a virtual object by moving it around. Typically, a VR system is composed of input/output devices, a computer and related software to integrate the information from the input/output device.[6,7] Higher demand for the computer is often required for fast real-time graphic information integration. The input tool could be sensors, controllers to capture the body movement. The output could be in visual, auditory, haptic, or even olfactory forms. A visual output device could be a monitor screen, head-mounted goggles, or a 3D projector depending on the immersive level. Audition and touch are mounted in the headset or in the form of controllers, which could provide vibration. As the immersive level increases, the user experiences a higher level of presence.

2. Applications in the healthcare domain

Besides entertaining media, the medical area has great potential for VR devices. In the past decade, medical applications of VR technology have been rapidly developing, and the technology has changed from a research interest to more commercially and clinically-based medical informatics technology.

2.1 Psychotherapy

Virtual reality can provide technical aid in autogenic relaxation, mental imagery, meditation, and other types of relaxation therapy to treat a variety of emotional disorders.

One example is in the treatment of anxiety. Studies have shown evidence that exposure-based treatment is the most effective among all anxiety treatments,[8] and VR can play an important role in creating the scene and providing a safe environment. This type of repeated exposure leads participants to consider feared situations less and less threatening and to experience less frequent feelings of anxiety.

Another application is in autism spectrum disorders (ASD). Minecraft, a non-VR game, has been found to evoke interest in children with ASD and engage them with their peers. Other games may be able to evoke similar interests. VR can add physical components to those games enabling them to learn motor skills in addition to social skills and entertainment.

2.2 Pain management

VR has great potential in treating pain as our understanding of pain perception is further advanced. Pain, which has been thought to be a response to tissue injury, is now perceived as a psychological phenomenon. The presence and severity of pain are determined in your brain and do not necessarily have to correlate with actual physical changes. Mirror therapy, graded exposure, and pain education have been studied to reeducate how the brain perceives pain and to maximally improve function in patients with complex regional pain syndrome, phantom pain, allodynia, hyperalgesia, fibromyalgia and other related diagnoses whose pathological cause are not fully understood.

Multisensory distraction is another application of VR under the principle of the pain management model. Activities combined with a multisensory VR system enhance the authenticity of the experience and can hence better divert the attention paid to pain. Documented areas of usage include wound care, cancer treatment, dental care, and transurethral prostate ablation to list but a few.

Research also suggests VR analgesia is accompanied by simultaneous reductions in pain-related brain activity in the cerebral cortex and brainstem.[9] VR analgesia has the equivalent magnitude to clinically relevant doses of opioid analgesics.[10]

3. Rehabilitation

Clinical rehabilitation is another promising application for VR technology that draws more and more attention each year. This chapter will discuss the benefits, applications, current studies, and considerations of using VR techniques in rehabilitation assessment and treatment.

3.1 Gaming and motivation

Motivation drives the duration and quality of the patient's treatment. For the field of rehabilitation, research has shown that games and related virtual technology can provide significant motivation.[11,12] Games are goal-oriented and evoke excitement, which will encourage a higher number of repetitions and active participation.[13]

3.2 Customized and tailored to individual need

Full control over the virtual environment and its configuration is another advantage of using VR technology in therapy. Specifically, VR allows factors such as speed, repetition, level of difficulty to be effortlessly and precisely manipulated while maintaining an objective means of data recording. The degree of freedom in customization in the virtual environment can allow gradual increments of difficulty and varieties.[14]

3.3 Low cost home-based training

To deliver a type of intensive, concentrated therapy is a challenge in today's clinical environment. The average length of stay in an inpatient acute rehabilitation facility is 14 days and 28 days for the skilled nursing facility.

One way to maximize the limited clinical resources is to shift physical therapist's role to a standby monitor or coaching role that empowers patient autonomy. Multitasking with several patients is manageable and efficient with the help of technology. Home-based VR exercise programs are also a viable option for patients who require continued rehabilitation to reach the targeted function; for those who require regular exercise and daily physical activity to maintain gains and prevent declines after outpatient rehabilitation; and for patients whose insurance coverage for structured rehabilitation is limited.[15,16]

Expenses spent in prop set-up, transportation, personnel reduced in a virtual environment and save the time and cost for both therapists and patients. As technology improves each day, the cost of VR devices and software are decreasing. It is not a dream to have home-based VR training at a relatively affordable price.

3.4 Combination of repetitive conventional therapy and virtual reality diversified training

Repetition is key to task-specific skill acquisition. Repetition training has better outcomes when tested under the same trained conditions. In other words, repetition enhances the stability of the performance. On the contrary of stability, variability training can enhance adaptability by enabling patients to transfer the learned skill from the training to related tasks and thus deal with variations in real-life scenarios.

Repetition training as conventional therapy is often compared to variability training, which involves a more varied protocol. Studies suggest variability training may engage more prefrontal and parietal regions[17] because each task requires the individual to reconfigure motor commands. Repetition training, however, allows for greater primary motor cortex excitability.[17]

VR training has the great benefit of simulating reality and providing many kinds of environments or scenarios. It embodies the idea of variable practice through a training schedule that includes frequent changes of task so that the participant is constantly confronting novel occurrences of the to-be-learned information. Apart from that, VR treatment itself adds a diversity into the patient's treatment plan, which may provide a challenge to the brain.

4. Examples of VR rehabilitation for neurological patients

4.1 Upper extremity (UE) training

In rehabilitation facilities, stroke, spinal cord injuries, traumatic brain injuries and other related neurological disorders are the main causes that lead to upper extremity dysfunction and have potential in VR training. Within a fully immersive VR environment, patients with strokes are a commonly studied group in VR experiments.[18] Research is often focused on upper extremity rehabilitation for safety considerations. In addition, the effectiveness of conventional interventions has generally been less pronounced for the upper extremity than for the lower extremity[19] which means multiple innovative treatment plans are expected to be discovered.

There are already several conventional treatment options available for patients who have a neurological disorder, with varied evidence to support them. The potential benefits of VR training are consistent with previous discussions. Repetitive task-specific training is commonly prescribed in stroke rehabilitation and has been shown to be effective for upper limb function, especially when higher doses are used. In animal models, 300-400 repetitions are needed in order to acquire a motor skill and to change the pattern of brain activity.[20] However, providing a high dose of therapy in rehabilitation is challenging considering limitations in insurance, human resources, and reduced length of hospitalization in reality. Moreover, patients may become less engaged or motivated after long and repetitive training[21]. Thus, alternative and innovative strategies are needed to resolve the problem of decreased efficiency over high dosage and the limitation for resources.[22]

Virtual reality interventions appear to be well suited for rehabilitation, as they provide concurrent feedback, can be tailored to match the person's ability[13,14], and can engage and motivate patients to achieve his or her therapy goals.[1,23]

A recent review examined 37 randomized controlled trials on upper extremity rehabilitation for a total of 1,019 participants with stroke.[22] Their results showed low-quality evidence that virtual reality is better than the same amount of conventional therapy for upper limb function and activity, with a small effect size based on 12 studies (397 participants). Subgroup analysis revealed a greater significant benefit for trials recruiting participants within six months of their stroke compared with more than six months after stroke. Nine trials (190 participants) either investigated virtual reality as an adjunct to conventional therapy or compared virtual reality with no intervention for upper limb function, and there was a significant effect in favor of the addition of virtual reality to conventional therapy. Furthermore, two trials (44 participants) evaluated the effect of virtual reality versus conventional therapy on hand function (grip strength), and three trials (60 participants) either investigated virtual reality as an adjunct to conventional therapy or compared virtual reality with no intervention on hand function (coordination). For both comparisons, there was no significant difference in grip strength between the groups.

From the previous results, it seems VR as an adjacent intervention is a promising treatment plan. This is consistent with the two hypotheses covered in the previous chapter, which are: variable training promotes skill transferability during motor learning; a high dose of task-specific treatment achieves the best treatment outcomes. However, despite the promising results in upper extremity rehabilitation in VR, the overall quality of data is low. Study sample sizes were generally small, with a lack of proper randomization or control groups. Some studies included inappropriate control groups that received no intervention compared to VR. The research outcome was hard to replicate due to varied interventions and customization. Bias was not consistently reported for further analysis. Interventions were predominantly designed to improve motor function rather than cognitive function or activity performance. The majority of participants were relatively young and more than one-year post-stroke. Thus, overall evidence remains "low" or "very low" quality when rated using the Grading of Recommendations Assessment, Development and Evaluation system.[22]

4.2 Hand dexterity

The most difficult task related to hemiparesis rehabilitation after a stroke is probably the recovery of the affected hand since the motor control tends to come back from proximal to distal. Since most commercially available VR gaming systems use two controllers for each hand to track upper limb movement, it is hard to free the hand and work on specific hand opening movement. Due to this difficulty, we will discuss hand rehabilitation as its own subcategory.

In order to free the hand but still tracking hand movement, an additional sensor by Leap Motion company (San Francisco, California) is available to mount on the front of VR goggles. The player will be able to see their segmented "skeleton hands" detailed to the level of each individual phalange. The same company also provides free games and applications that specifically target rehabilitation needs. An example game is called "Block" in which the player has to demonstrate fine motor control of the hands to manipulate basic virtual blocks such as grabbing them, stacking them, moving palm up or palm down together with pointing, pinching and opposition.

Several studies show promising results using Leap Motion VR training for neurological patients.[24–26] In Wang et al.[25] with the randomized experiment among patients with subacute stroke, the study group was treated with conventional therapy plus VR training, while the control group only did conventional therapy. After four weeks of treatment, the motor functions of the affected upper limbs were significantly improved in both groups, but the improvement in the study group was significantly better than in the control group. The action performance time in the Wolf Motor Function Test significantly decreased in the study group. This study shows the feasibility of combining VR in conventional therapy for fine motor rehabilitation in the hand.

4.3 Lower extremity (LE) VR training

There are relatively fewer studies investigating the lower extremity compared to the widely researched VR potential in upper extremity rehabilitation partially because of the safety concern and partially because of the difficulties in tracking moving with lower extremities. However, lower extremity VR training is increasingly popular with new technology like 3D projection. As with the UE, there are similar concepts of LE strength and range of motion (ROM) training. Similar movement tracking sensors are mounted on each foot. Participants could complete activities such as kicking, juggling balls, stepping on virtual hamsters, driving a virtual car in a seated or standing position while working on ankle, knee, and hip movements.

Balance and gait activities are also common themes in LE VR training which often involves a treadmill with 3D projection. The immersive level could range from 1) non-immersive VR in which virtual images generated by the computer are projected in front of the user either on a screen or on a wall; 2) semi-immersive which virtual images are overlaid onto real images increasing the informative content of the real world; to 3) immersive VR in which the viewer is part of the environment often with a head-mounted display. Immersive systems are perceived to be more effective because they provide a more intense feeling of reality; however, they may cause motion sickness in some participants.

Cochrane systematic review[27] on patients with stroke provided evidence for a stronger effect of VR training compared with conventional therapy, as suggested by the significantly greater improvements in balance and gait ability. Gait speed, Berg balance score, and Timed Up and Go test were the most frequently used measures to underpin the stronger effect of VR training. However, more well-designed studies need to be done to confirm the research findings.

5. Knowledge gap

A search of the Cochrane library database shows systematic reviews of virtual reality in participants with stroke and Parkinson's disease.[27] While there are other studies using VR on a variety of neurological diagnoses, stroke seems the major studied population. A search of "stroke AND virtual reality" yielded a total of 270 papers. The same search yields only 52 papers for Parkinson's disease, 22 for spinal cord injury (SCI), and 20 for traumatic brain injury (TBI). Motor learning and neurological principles could be generalizable to those disorders. Future investigations of a variety of related neurological disorders could potentially broaden the scope of practice for VR and provide insight into subgroup comparison of what population benefits from VR the most.

Asides from diagnoses, presentation in motor skills, pain, spasticity, coordination could vary even within one diagnosis group. Thus, further investigation into a more defined level of impairment needs to be done in order to provide a guideline for the use of VR in rehabilitation.

As discussed, the reviewed articles do not allow participants to choose games themselves and could potentially lead to a drop of enthusiasm over time, depending on the duration of treatment.

Rigorous research designs provide good internal validity. However, it is also important to verify whether the treatment outcome from a laboratory could transfer to a clinical setting. Utilizing commercially available VR would be a good option for front line clinicians to apply VR into their daily practice without the increased burden of customizing and optimizing a system. Cochrane review[27] also suggests that the type of device (commercial or customized) would not affect the treatment outcome. Thus, it is meaningful and promising to conduct a feasibility test of commercially available VR in a clinical setting in order to explore external validity.

The value of VR intervention goes beyond motor skill learning. Psychological parameters could improve with treatment. Participants' mental health needs to be addressed, especially for limited mobility, presentation of pain after a huge life change. VR, as an advanced reality re-creation technology, could help in psychotherapy such as autogenic relaxation, pain distraction. It is an alternative tool for them to wander in the outside world which otherwise would be impossible due to physical limitation. With those in mind, further investigations are promising and necessary in order to explore the multiple potentials VR can bring to neurological populations.

6. Summary

With further technology development, applications of VR have huge potential in both the clinical and research domains of rehabilitation. Further evidence-based studies with control groups are essential to demonstrate their efficacy as compared to conventional treatment. Standardized protocols and objective measurements are needed to generalize and replicate research outcomes in broader settings.

Chapter Two: The Case Series

Introduction

According to a new estimation, there are about 17,730 new spinal cord injury (SCI) cases in the United States each year.[28] To put it into perspective, that is approximately 54 cases per one million people in the United States. Symptoms of spinal cord injury depend on the severity of injury and its location on the spinal cord. After the incident, symptoms may include partial or complete loss of sensory function or motor control of arms, legs and/or body. Pain, depression and loss of coordination can be secondary to the sensory and motor dysfunctions. These impairments cause limitations in mobility, self-care and ultimately impact an individual's family and social life. Several treatment options are available to regain and maximize function. Repetitive task-specific training has been shown to be effective for improving walking and upper limb function, especially when higher doses are used.[12,20,29] However, a high dose of therapy and accurate representation of real-life stimulation are challenging due to limitations in staffing, resources and length of hospitalization. Moreover, participants may become less engaged or motivated after long and repetitive training sessions[21]. Thus, alternative and innovative strategies are needed.

Virtual reality (VR) is an emerging treatment option, and has been defined as the use of interactive simulations created with computer hardware and software to present users with opportunities to engage in environments that appear and feel similar to real-world objects and events.[1] It provides concurrent feedback, and can be tailored to match the person's ability.[14] Incorporating the literature with our own hypothesis, we think the real life simulation and personalized design could help stimulate more senses that contribute to a better training outcome.

Second, the daily task basis and game format can engage and motivate participants to achieve their therapy goals. Third, VR may have the capacity to provide a high dose of repetitive task-specific training. Last, VR intervention was also found to reduce spasticity[30,31] which could improve functional mobility.

Apart from the potential benefits for physical rehabilitation, VR may have some positive effects psychologically[32] and potentials to reduce pain.[9,10] As patients go through some serious and potentially permanent changes, VR could still enable them to wander freely in an imaginary world. It could provide an outlet for their real-life anxiety and depression.

Research in this area shows limited evidence that VR is better than the same amount of conventional therapy for upper limb function and activity, with a small effect size.[22,27,33] Investigations into VR as an adjunct to conventional therapy for upper limb function shows significant effect in favor of combination of VR and conventional therapy compared to conventional therapy alone.[18,34]

VR research is still in an early stage, this case series provided more evaluations of VR in a more defined patient population. It also tracked the process of training and hopefully provide more improvements of the VR design. Moreover, it collected participant's feedback and attitudes toward this new intervention and provided some useful information for its practice in hospitals or clinics. The purpose of this case series was to 1) evaluate the feasibility of using a fully immersive and commercially available VR device in a subacute inpatient clinic for UE rehabilitation in patients with neurological disorders; 2) compare training effects among participants; 3) evaluate participant's response and feedback from qualitative data. We hypothesized that participants would demonstrate improved functional outcomes and demonstrate high motivation and enjoyment with the conjunction of VR intervention.

Method: intervention, measurements

For standardized outcome measurements, we chose strength as well as functional tests as markers for progress. Because strength loss is a common presentation after spinal cord injury, we chose muscle strength testing as one of the outcome measurements. In the performance of fine motor skills, strength, spasticity, proprioception, sensory input, coordination, and motor control all interact with each other in upper extremity (UE) functions. To capture UE function, the 9-hole peg test was used.

Outcome measurements for muscle strength tests included scores for seven manual muscle tests (shoulder flexors and abductors, elbow flexors and extensors, wrist extensors, finger flexors and abductors). The seven scores were added for a composite score. Each "+" level of strength was calculated in half point increments on the 0-5 manual muscle testing scale. For example, a 3+ MMT =3.5 on the composite score. Grip strength and key pinch strength were measured with handheld standard dynamometry. The average of 3 measurements were taken as the final score. Minimally clinically important differences for grip strength in the stroke population are 5 kg (11.02 lbs), 6.2kg (13.67 lbs) for the affected dominant and non-dominant side.[35]

We chose the 9-hole peg test to measure functional gains. This is a timed test where the participant is asked to take the pegs from a container, one by one, and place them into the holes on the board, as quickly as possible. Normal completion times is between 17.54-17.71 seconds for the right hand among healthy men in the age group of 31-40 years old.[36] The minimum clinical importance value of this test in the stroke population is 32.8 seconds.[37]

All four tests were taken initially as a baseline and every other week after the start of intervention by clinicians in the treatment team. A questionnaire regarding the participant's experience with VR training was administered at the end.

Baseline data included all the outcome measurements except the final questionnaire which was completed after the intervention. Mini Mental Status Examination (MMSE) was used for all participants as an indicator for cognitive function. The MMSE test includes simple questions and problems in a number of areas: the time and place of the test, repeating lists of words, arithmetic such as the serial sevens, language use and comprehension, and basic motor skills with a possible score of 30. This tool is used to provide a picture of an individual's present cognitive performance based on direct observation of completion of test items/tasks. A score of less than 24 is generally the accepted cut off indicating the presence of cognitive impairment. Impairment have been classified as three levels: No impairment: sore=24-30; Mild impairment: score 18-24; Severe impairment: score=0-17.[38,39]

Intervention

Each participant received a 30-minute VR treatment twice/week plus regular physical therapy and were followed for at least 2 months till discharge. The VR equipment in this project is a commercially available headset, Oculus Rift (Oculus VR, LLC, San Francisco, California), which is non-FDA approved equipment. Most software is free to download and use when we purchased this equipment. Using this commercially available product enables clinicians to apply the technology in their practice without the need for in depth training in programming.

In the VR training sessions, participant wore a pair of goggles which generated a virtual environment. Audio was available through the internal headphone attached to the goggles. Since the goggles completely blocked vision and put the participant in an immersive environment, this type of experience provides the highest level of presence in the virtual world.

Add-on sensors (Leap Motion, Inc., San Francisco, California) on the goggles could capture their hands and arms movements and interactively present their movements in the virtual world. Games and tasks were available for participants including moving virtual objects, pinching candles, and stacking virtual objects. Participants did not physically get up and walk around but remained seated throughout the intervention.

Bilateral controllers with thumbsticks and buttons were used in certain games to simulate weapons or tools. It was also used as a controller to choose games and change settings.

In addition to the study interventions, conventional therapies such as fine motor training/coordination and functional grip strength training were practiced following the typical clinical protocols of the rehabilitation center.

Game analysis

Games used with the Oculus Rift VR equipment are categorized into 4 groups depending on the level of the participation in the virtual world.

Level 1

The first level of play is headset only. Participants are provided with visual and auditory stimulus to sustain attention and increase cognition function. At this level, participants only need to hold their heads up and have certain neck motion to look around. No motor skills in the upper extremity are required to participate. Games are often in a story telling format or travelling with a first person angle. See Table 1 for an example of a Level 1 game.

Table 1: Sample of the Level 1 Game

Game	Discovery VR		
Description	Walk on the African savannah, swim with sharks in the ocean, explore in the jungle		
Mobility Requirements	**Neck:** -Flexion -Extension -R/L rotation		
Vision, Cognition & Physical	**Cognitive:** -Sustained Attention	**Vision:** -Visual scanning -Visual acuity -Eye teaming	**Physical:** -Static balance -Gross motor control
Precautions/ Contraindications	-Motion Sensitivity -Auditory Sensitivity -Visual Sensitivity		

Level 2

Second level includes the use of a headset and the hand tracking sensor--Leap Motion. With Leap Motion, hand motion can be tracked in real time and participants are able to see their real hands virtually in the simulated environment allowing them to interact with objects in the virtual world. The virtual hands appear in a skeletal format, but each digit and joint movement is isolated and corresponds to the movement of their real hands. Participants engage in the game with their hands such as picking up a virtual object in the virtual world. Note that there is no real weight in their hands when they are interacting with virtual objects which could make functional activity such as lifting a cup easier than in real life.

Table 2: Sample of the Level 2 Game

<table>
<tr><td>Game</td><td colspan="3">Blocks</td></tr>
<tr><td>Description</td><td colspan="3">Game that uses Leap Motion to have the user create different shapes and move them around in the environment. Tutorials are provided in the game and users are asked to follow the lead of the robot tutor.</td></tr>
<tr><td rowspan="2">Mobility Requirements</td><td>Neck
-Flexion
-Extension
-L/R Lateral Rotation</td><td>Elbow
-Flexion
-Extension
-Supination
-Pronation</td><td>Hand
-Finger Extension: MCP, PIP, DIP
-Finger Flexion: MCP, PIP, DIP
-Thumb abduction/ adduction
-Opposition</td></tr>
<tr><td>Shoulder
-Flexion
-Extension
-Abduction
-Adduction
-Horizontal Abduction
-Horizontal Adduction</td><td>Wrist
-Radial Deviation
-Ulnar Deviation
-Flexion
-Extension</td><td></td></tr>
<tr><td>Vision, Cognition & Physical</td><td>Cognition
-Sequencing
-Cause and Effect
-Problem Solving
-Motor Planning
-Sustained Attention
-Hand eye Coordination</td><td>Vision
-Visual Scanning
-Acuity
-Eye Teaming
-Depth Perception</td><td>Physical
-Crossing Midline
-Proprioception
-Bilateral Coordination
-Dynamic Balance
-Finger Isolation
-Maintaining Sitting/ standing balance
-Finger Opposition</td></tr>
<tr><td>Precautions/ Contraindications</td><td colspan="3">-Motion Sensitivity
-Auditory Sensitivity
-Visual Sensitivity</td></tr>
</table>

Level 3

Third level includes the use of headset and handheld controllers. Participants need to hold up the controller at this level. There is no need to use the button or thumbstick on the controller. Controllers can provide extra tactile cues of vibration when the participant achieves their target in the game.

Table 3: Sample of the Level 3 Game

<table>
<tr><td>Game</td><td colspan="3">Beats Fever</td></tr>
<tr><td>Description</td><td colspan="3">Beats Fever is a VR rhythm game where players enjoy stylish music and catch incoming notes with 2 controllers in both hands. The controllers will vibrate when you hit or slide on the notes as a positive feedback. Incoming notes are guided with visual display. Each hand has its own notes to catch and needs to coordinate with the other in order to maximize the catch.</td></tr>
<tr><td rowspan="2">Mobility Requirements</td><td>Neck:
-Flexion
-Extension
-L/R Lateral Rotation</td><td>Elbow:
-Flexion
-Extension
-Supination
-Pronation</td><td>Hand:
-Gross Grasp</td></tr>
<tr><td>Shoulder:
-Flexion
-Extension
-Abduction
-Adduction
-Horizontal Abduction
-Horizontal Adduction</td><td>Wrist:
-Radial Deviation
-Ulnar Deviation
-Flexion
-Extension</td><td></td></tr>
<tr><td>Vision, Cognition & Physical</td><td>Cognition:
-Cause and Effect
-Problem Solving
-Motor Planning
-Hand Eye Coordination
-Sustained Attention
-Divided Attention</td><td>Vision:
-Visual Scanning
-Eye Teaming
-Peripheral</td><td>Physical:
-Dynamic Balance
-Crossing Midline
-Proprioception
-Bilateral Coordination
-Endurance
-UE coordination
-Reaction time</td></tr>
<tr><td>Precautions/ Contraindications</td><td colspan="3">-Auditory sensitivity
-Visual sensitivity
-History of Epilepsy
-History of Seizure
-Fatigue</td></tr>
</table>

Level 4

Fourth level is the highest level. Participants need to hold the controller plus push buttons, triggers or manipulate the thumbstick in order to activate certain features in the experience. Fine motor control and hands coordination are challenged.

Table 4: Sample of the Level 4 Game

<table>
<tr><td>Game</td><td colspan="3">Ready, Aim Splat!</td></tr>
<tr><td>Description</td><td colspan="3">In this experience, users are required to put their slingshot skills to the test and stop the oncoming horde of zombies. With 2 controllers at each hand to stimulate the sling on the left and the shot on the right, users could shoot vegetables at emerging zombies from 360 degree. As the levels go up, the scenarios will get more complicated with more zombies appearing from the ground, and faster speed to approach the user and more unexpected directions</td></tr>
<tr><td rowspan="2">Mobility Requirements</td><td>Neck:
-Flexion
-Extension
-L/R Lateral Rotation</td><td>Trunk:
-R/L Lateral rotation</td><td>Wrist:
-Flexion
-Extension</td></tr>
<tr><td>Shoulder:
-Flexion
-Extension
-Abduction
-Adduction</td><td>Elbow:
-Flexion
-Pronation
-Supination
-Extension</td><td>Hand:
-Gross grip
-Finger flexion</td></tr>
<tr><td>Vision, Cognition & Physical</td><td>Cognitive:
-Cause and Effect
-Problem Solving
-Motor Planning
-Sustained/ Divided Attention</td><td>Visual:
-Visual Scanning
-Acuity
-Eye Teaming</td><td>Physical:
-Sitting balance
-Bilateral coordination</td></tr>
<tr><td>Precautions/ Contraindications</td><td colspan="3">-Motion Sickness
-Visual Sensitivity
-Auditory Sensitivity
-History of Epilepsy
-History of Seizure
-Fatigue
-Fear of thrilling content</td></tr>
</table>

Case Presentation A

History and course of rehabilitation

Participant A was a 39 y/o male, with a history of C5 ASIA B non-traumatic spinal cord injury following a spinal cord stimulator placement to wean from narcotic and muscle relaxants. This produced excellent management of his lower back pain until he developed generalized numbness and weakness 8 months later. Magnetic Resonance Imaging demonstrated a high grade narrowing at C4-C5 resulting in the participant having a C4-5 anterior cervical discectomy and fusion. Initial ASIA Impairment Scale score was C5 ASIA B with a C6 motor level on the right. He went to an acute rehabilitation unit and then transferred to subacute rehabilitation for continued therapies.

During a life coach meeting, he reported that being a father, husband, gamer, and employee gives him purpose in life. Because of the injury, participant A is exploring his adaptive technology options focused on building skills towards resuming his role as a software developer. He is highly interested in smart home devices and virtual reality to augment his rehabilitation.

Baseline data

A scored a 26/30 score in the Mini Mental State Examination (MMSE) which suggests no cognitive impairment. He had a 14.5/35 composite manual muscle testing score for the left upper extremity key muscles and a 19.5/35 for the right. He had 0 lbs grip or pinch strength and was not able to perform the 9-hole peg test on the left hand. On the dominant right side, he finished the 9-hole peg test in 5 minutes. See Table 5 for participant A data.

Functional mobility and therapeutic goals

Participant A used his own personal Permobil power wheelchair for all functional mobility. He was independent with driving, pressure relief, and repositioning.

Physical therapy and occupational therapy goals include: 1) Improving to modified independence for upper body dressing and maximal assistance with lower body dressing, and 2) Improving his upper extremity strength and dexterity to open and manipulate packages during meal preparation in the kitchen.

Participation

Participant A started with the level 1 VR games and was fascinated by the presence of the virtual world. He had no history of epilepsy and reported no motion sickness from the level 1 game. He moved up to higher level games after the first visit. Considering his weakness in both hands and his goals to improve fine motor control in his hands, “Blocks” with Leap Motion sensor was the best fit to work on functional activities such as pinch, grasp, point, stack objects, thumb up, palm up/down in a non-weight bearing manner. A robot in the game provides the participant with a tutorial and interaction in the game. Then the player is left to his own creativity. As he became more familiar with the game, the therapists needed to come up with new tasks in order to keep him engaged and challenged. “Beats Fever” was also added to promote bilateral reaching activities in all directions due to general weakness in the shoulder musculature. In this game, he had to reach for the “notes” that constantly fly at him on the rhythm of the music. General grip is needed in order to hold the controllers but there is no need to use the buttons, triggers or thumbsticks. This game is often described as an “arm workout” by participants given its high intensity and relatively long duration. Participant A was challenged with a high paced, complex bilateral reaching pattern and dual tasking with both hands reaching in different directions at the same time. Visual scanning for upcoming “notes”, bilateral coordination, motor planning, and divided attention are intuitively deployed to advance the performance. Songs are also varied in difficulty level.

As he progressed, more variety of games were added in his training. “Weightless” is a level 2 game with Leap Motion sensor. The main movement is to pinch, grasp an object and toss it to a target with the same color. Carnival is a level 4 game that includes a series of carnival games. Controllers are used to stimulate tools or hands in scenarios of archery, ring toss, gun shooting, “Whac a mole”, and basketball shoot. Main movement includes flexion/extension of thumb, index, and ring finger, wrist flexion/extension and shoulder flexion/abduction. Grasping is indirectly realized by pushing into the 2 triggers on the side of the controller with index and ring fingers leaving the thumb available to manipulate the buttons for other functions. The ergonomic design enables participants to use the controllers in a natural way for manipulating objects. Participant A had a great passion to discover new games and we explored more games in different contexts or themes to keep him engaged as we progressed. The movement components are similar to the games discussed above.

VR could be a safe intervention for him when used properly. He experienced motion sensitivities for a specific game once when the picture was not in sync with his motion. The noticeable lag was the main cause of his motion sensitivity. This prompted us to remove the game from our protocol. He also experienced an episode of hypotension after fatigue. This did not appear to be any more frequent than with other conventional interventions. He was acquainted with dealing with his episodes of hypotension from past experiences by reclining back in his power wheelchair. Rest and water would be offered after visible fatigue during sessions.

Participant A had a good participation rate and was challenged throughout the study. Less than 5 cancelations were due to either an episode of urinary tract infection or unknown discomfort. His family, including his son and wife, were welcomed to watch and interact with him during the intervention. He expressed that he used to play video games prior to his injury, and he would consider VR as a new alternative to interact with his son in the future. He also mentioned the intention to purchase a VR device after discharge.

Results

Table 5: Participant A Data

Participant A	31-May		9-Jun		21-Jun		10-Jul	
	L	R	L	R	L	R	L	R
Finger Flexor	1	2	1	2	1	2	1	2
Finger Abductor	0	2	1	2+	1	2+	1	2+
Wrist Extensor	1	2	1	2	2	2+	2	2+
Elbow Flexor	5	5	5	5	5	5	5	5
Elbow Extensor	2	3	2	3+	2	3+	2	3+
Shoulder Flexion	3	3	3	3	3	3	3	3
Shoulder Abduction	2+	2+	2+	2+	3	3	3	3
Composite	14.5	19.5	15.5	20.5	17.0	21.5	17.0	21.5
Grip (lbs)	0.0	4.7	0.0	5.3	0.0	9.7	0.0	10.7
Key Pinch (lbs)	0.0	0.0	0.0	1.0	0.0	2.0	0.0	4.3
9-Hole Peg (s)	-	300.0	-	136.0	-	53.7	-	58.1

- Unable to perform

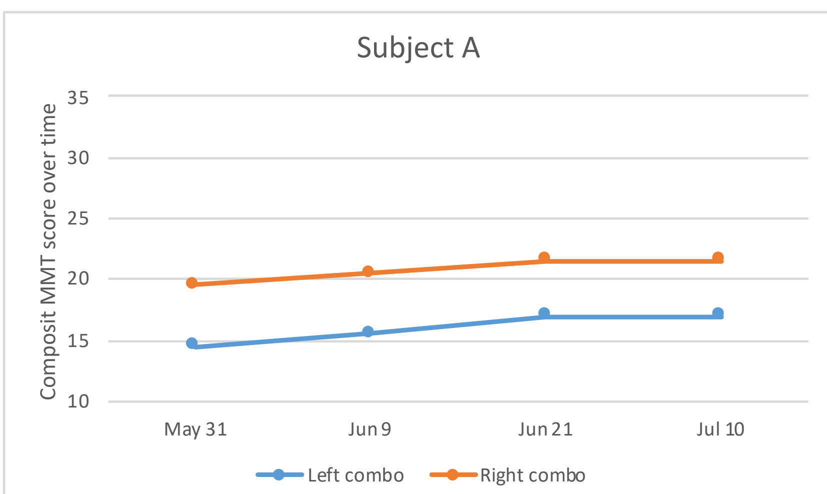

Figure 1: Participant A Composite MMT over Time

Discussion

Participant A's main goal was to increase strength and control of wrists and fingers, especially on the left side. As seen in Table 5, in the composite MMT scores, he did not show great improvement, with a 2.5-point change for the left side and a 2-point change in the right side. Grip and pinch score changes did not approach a level of significance either, but functionally he had made visible improvement. Manual muscle testing or other strength tests may not be sensitive enough to catch the functional change and may not necessarily translate to performance especially for small but refined motions in the hands. At the end of the study, Participant A could hold the controller without the use of Velcro tapes whereas in the beginning of the study his hand was too weak to hold the controller in place without Velcro tapes. However, he remained unable to perform the 9-hole peg test on the left side in the end, meaning that fine motor control was still lacking. This is not surprising since the design of many games have lateral differences. The right hand tends to be used as the main action and the left hand is used as facilitation. For participant A, this seemed to work well since he had really low function on the left side. If his right side was as weak as the left, he would not be able to participate in level 3 and above games. As another example of laterality impacting outcome, there was a clinical meaningful change of the 9-hole peg test for his right hand, from 5 minutes at baseline to 58.07 seconds before discharge. The results far exceeded the minimum detectable change of this test.

Case presentation B

History and course of rehabilitation

Participant B is a 37 y/o male with non-traumatic spinal cord injury secondary to congenital spinal stenosis, most affected in C5 level. Participant B demonstrated tetraparesis with Brown-Sequard Syndrome distribution in the upper extremities. His right upper extremity demonstrated the most function.

Participant B began having symptoms in his upper extremities that eventually over five months involved his bilateral lower extremities in terms of numbness and weakness related to congenital spinal stenosis. He underwent a surgery for herniated discs at C3-7 and a partial discectomy at C5. Post-operatively, participant B participated in a comprehensive acute rehabilitation program then transferred into a subacute rehabilitation center with the goal of returning to community-based living.

Baseline data

Participant B scored a 24/30 score in the Mini Mental State Examination (MMSE) which suggests no cognitive impairment.

He had a 18/35 composite manual muscle testing score for the left upper extremity key muscles and a 24/35 for the right. He had 10.67 lbs grip, 0 lbs pinch strength and was not able to perform the 9-hole peg test on the left hand. On the dominant right side, he had 33 lbs grip, 8 lbs pinch strength and finished the 9-hole peg test in 66 seconds. See **Table 6** for participant B data.

Functional mobility and therapeutic goals

Participant B utilized his own personal power wheelchair for all functional mobility. Mild tone/spasticity was present in his chest/abdomen and bilateral upper and lower extremities.

Participant B also demonstrated flexor synergies in reaching activities which are characterized by scapular retraction and elevation, shoulder abduction, elbow, wrist and finger flexion.

Physical therapy and occupational therapy goals include improving his upper extremity abilities and strength to allow him greater independence in dressing, grooming, bathing and toileting tasks. Specifically, his goals were minimal assistance with upper body dressing and moderate assistance with lower body dressing.

Participation

Participant B started with the game “Beats Fever” to work on shoulder ROM and strength which didn’t need any wrist or hands motion. He had no problem holding on the controllers. “Beats Fever” remained as part of his intervention throughout the training as an arm workout activity. Patterns in reaching activities were rhythmic and competitive, he was challenged and engaged throughout the study. Flexor synergies in both UEs made it difficult for him to reach with his arm while opening up his palm. “Blocks” with Leap Motion sensor was also introduced at the early stage to work on the fine finger movement such as pinching, pointing, grasping and manipulating objects. As he progressed, more games were explored including several with mission completion. “Bullet train”, a first-person shooting game in which scenes constantly move forward in the direction of vision at a set speed as if players are moving in the game to discover new scenes. This is a good game for participants who cannot tolerate standing and walking in a real environment for safety concerns but also give them first person perspective by allowing head turns to control direction of movement. This is a level 4 game in which buttons and triggers are needed for picking up weapons, shooting targets, and activating special skills such as teleportation or time manipulation. The right hand was the dominant hand for action execution while the left was the assisting hand. For optimal performance participant B could also hold one weapon in each hand and multitask but it was challenging due to the time limit in the game.

The game “Pro fishing” was added to his program to improve the quality of performance in tossing and throwing with a focus to reduce compensation movements and synergies. This is a level 4 game in which controllers are needed. Stimulation of hands for grasp is still natural by squeezing the side triggers around the holding bar. This game has laterality for hands, with the right hand used for casting and the left hand for reeling. Participant B performed a combination of movements on his right UE in order to cast as far as he could to perform wrist pronation and elbow extension together with shoulder flexion and rotation. This game helped practice fluidity in movement and was selected to decrease abnormal synergies and reduce spasticity in the UEs. For the left hand, repetitive wrist supination and pronation were practiced during reeling activity. The controller also provided him a vibration to simulate weight on the reel. Participant B also participated in other level 4 games such as “Spider Man” and “Carnivals” for fine motor control.

Results

Table 6: Participant B Data

Participant B	9-Jun		23-Jun		5-Jul		21-Jul		9-Aug	
	L	R	L	R	L	R	L	R	L	R
Finger Flexor	0	1	0	1	2	3	2	5	3	5
Finger Abductor	1	2	1	2	1	2	2	3	2	3
Wrist Extensor	3	5	3	5	3	5	4	5	4	5
Elbow Flexor	4	5	4	5	4	5	5	5	5	5
Elbow Extensor	4	5	4	5	4	5	3+	5	3+	5
Shoulder Flexion	3	3	3	3	3	3	2+	5	2+	5
Shoulder Abduction	3	3	3	3	3	3	2+	5	2+	5
Composite	18.0	24.0	18.0	24.0	20.0	26.0	21.5	33.0	22.5	33.0
Grip (lbs.)	10.7	33.0	9.3	39.0	7.0	47.3	9.7	42.3	14.3	50.0
Key Pinch (lbs)	0.0	8.0	0.0	8.0	3.0	8.0	0.0	6.3	3.0	10.0
9-Hole Peg (s)	-	66.0	-	62.0	60.0*	66.0	121.0**	51.6	69.0	46.6

* Picked 2 pegs in 60 sec, not able to finish the test
** Modified by handing pegs to his hands
- Unable to perform

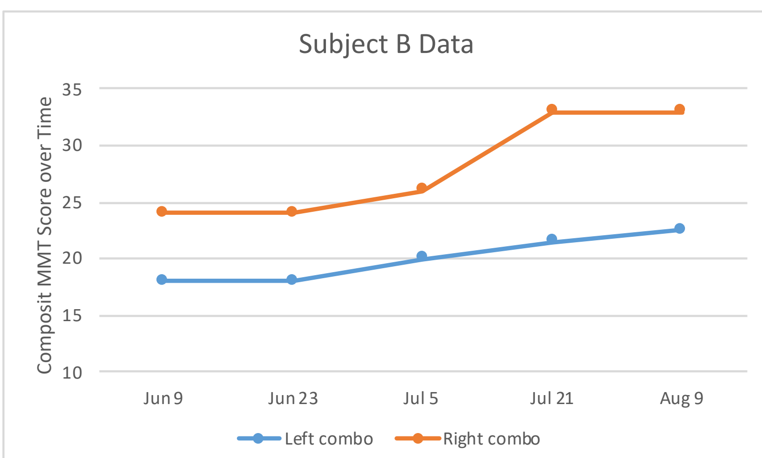

Figure 2: Participant B Composite MMT over Time

Discussion

The main goals of participant B's VR intervention were to reduce spasticity, improve strength, and improve fine motor control in the fingers in functional activities. Rationale for game selection was different from participant A given his spasticity and synergies. Participant B also had relatively higher function compared to participant A, especially in terms of strength which allowed him to play a broader range of games. Participant B had an overall 13.5-point change in bilateral MMT composite scores which was the biggest change among the three participants. The biggest change came from the finger flexion bilaterally. The right UE had 9 points of change in MMT composite score whereas the left UE only had 4.5 points. This difference could have resulted from the laterality in game designs as we discussed previously. The right hand was also favored because he had the most function reserved on the right side. Given the Brown-Sequard distribution, spasticity in the right UE may have allowed him to more quickly respond to therapy and medications compared to the true strength deficit on the left hand.

As we discussed in case A, strength tests may not be sensitive enough to catch all the improvements, especially functional gains in lower level participants. The left UE demonstrated clinically meaningful improvement in functional tests despite lesser improvement in MMT composite scores compared to the right. The left hand was not able to perform the 9-hole peg test at baseline. At week 4 he could pick up 2 pegs in 1 min but still could not finish the test. At week 6 he could finish the modified version of the test in 2 min which the pegs were handed to him and he would put them in the holes. In the final test, he finished the full version of the test in 69 sec. This is a clinically meaningful change compared to the 32.8-second minimum detectable change of this test in the stroke population. For the right UE, 9-hole peg test improved 20.6 sec to 46.6 seconds. This score was still below normal values in the healthy population within his age group[36], therefore we speculate he plateaued his rehabilitation potential on this test given the clinically meaningful improvements in strength but not in functional tests for the right side. Since the VR environment would highly simulate reality, high transferability into functional tasks was expected.

Case presentation C

History and course of rehabilitation

Participant C is a 37 y/o male, with a history of traumatic spinal cord injury after a motor vehicle accident (MVA). Initial imaging showed left-sided C6-7 locked facet with various fractures from C7-T10 resulting in a fusion at C6-7. At the inpatient rehabilitation facility, he was neurologically classified as an ASIA C. After four months, he began subacute rehabilitation with the goal of returning to community-based living in the future.

Baseline data

Participant C scored a 24/30 score in the Mini Mental State Examination which is the minimum score for the classification of no cognitive impairment. Participant C initially had almost a full MMT composite score, at baseline 30/35, and 35/35 for the left and the dominant right side respectively. His grip strength was 43.6 lbs for the Left, 70.3 lbs for the Right and pinch strength was 10 lbs for the Left and 8.6 lbs for the Right. The 9-hole peg test was 38.2 sec and 29.6 sec for Left and Right respectively. See Table 7 for participant C data.

Functional mobility and therapeutic goals

Participant C used a manual wheelchair for mobility. He demonstrated extensor spasticity in the lower extremities. He also had a history of ankylosing spondylitis with residual pain in his lower back and pain in his neck and left shoulder during functional mobility. The therapy goals were as follows: 1) modified independence bathing when set up with his supplies and adaptive equipment; 2) modified independence in dressing with set up; 3) return to driving, with hand controls; 4) pain management. It was hypothesized that virtual reality training as a pain-relief strategy could be used in addition to increasing the fine motor control of his left hand.

Participation

Participant C started with the “Beats Fever” which is one of the most intuitive games in our selection to get used to the VR device and also to work on elbow strength. Participant C showed good UE strength while performing this game, but as the patterns got more complicated and speed got faster, it was still challenging for him to be accurate for both UEs at the same time. Participant C was then introduced to “Pro Fishing” which works on forearm supination and pronation as well as some finger movements with thumbstick and buttons activation. This was not a high intensity game for him given his almost full strength in bilateral UEs. However, as he proceeded through the study it was evident that he really enjoyed boating, fishing prior to the injury and this game would be of interest. He expressed a feeling of serenity and excitement of fishing in the game.

Leap Motion games such as “Blocks” and “Weightless” were also included in the program at an early stage to work on fine motor control in the fingers. He was amazed how real the hand tracking was and enjoyed the possibilities of interaction in the virtual world. However, the games were not challenging enough for him to get to a therapeutic threshold. He also worked on level 4 games such as “Bullet Train”, “Ready, Aim, Splat!”, “Echo VR”, “BBC Spacewalk”, and “Spiderman Homecoming” in which storylines and scenarios were unique and captivating.

Results

Table 7: Participant C Data

Participant C	6-Jun		20-Jun		7-Jul		21-Jul		8-Aug	
	L	R	L	R	L	R	L	R	L	R
Finger Flexor	4	5	4	5	4	5	5	5	5	5
Wrist Flexor	5	5	5	5	5	5	5	5	5	5
Wrist Extensor	5	5	5	5	5	5	5	5	5	5
Elbow Flexor	5	5	5	5	5	5	5	5	5	5
Elbow Extensor	4	5	4	5	4	5	5	5	5	5
Shoulder Flexion	5	5	5	5	5	5	5	5	5	5
Shoulder Abduction	5	5	5	5	5	5	5	5	5	5
Composite	33.0	35.0	33.0	35.0	33.0	35.0	35.0	35.0	35.0	35.0
Grip (lbs)	43.6	70.3	44.3	68.0	45.7	65.3	50.0	71.3	50.0	70.0
Key Pinch (lbs)	10.0	8.6	9.0	8.7	11.0	9.0	10.3	6.7	12.0	9.0
9-Hole Peg (s)	38.2	29.6	31.7	27.5	34.1	27.9	30.4	32.0	29.8	26.7

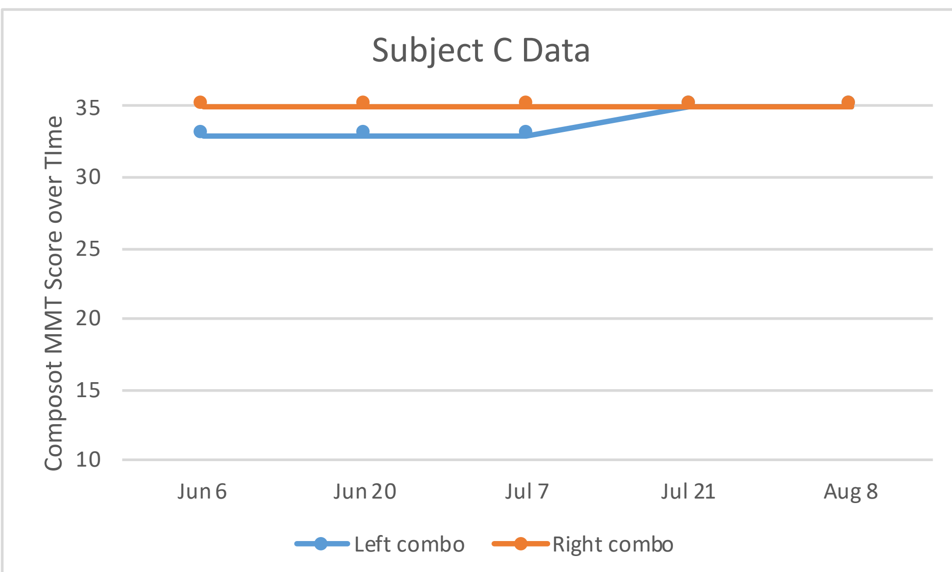

Figure 3: Participant C Composite MMT over Time

Discussion

Participant C was enrolled in the study because of his interest in technology and gaming. Participant C had relatively higher UE functional ability compared to the other two participants enrolled. He had 5/5 manual muscle testing scores at baseline except for the left elbow extensor and left finger flexor. Our rationale for him was to reduce pain and release stress, in addition to increasing functional mobility in the UEs, and thus impact his independence in activities of daily living and return to driving.

"Beats Fever" was selected as a high intensity upper extremity work out with motor planning and bilateral UEs coordination. This game remained very helpful throughout his intervention. A series of level 4 games were chosen to improve finger flexion and thumb abduction. Those high-level games were designed for the normal population with captivating scenes and plot. Movement with holistic control, not only exercising coordination between fingers and between hands but the whole upper extremity, for example, triggering the button with throwing activities in the "Spiderman Homecoming" game. By the end of the study, participant C achieved 5/5 muscle strength bilaterally and slight increase of grip and pinch strength for the left hand. The 9-hole peg test improved by 8.3 seconds for the left and 2.9 seconds for the right. None of those changes reached clinically meaningful levels. This could be attributed to his high initial scores, especially on the right side.

It was difficult with these games to realize strengthening because there is no additional weight added. The advantage of manipulating weightless objects in the virtual world didn't allow for strength training for high functional level participants. On the contrary, speed, ROM, motor planning, and coordination which are highly incorporated in VR games were not adequately captured by the 9-hole peg. We suspect that gaming would benefit him in hand controls of his driving program. During the course of the study, there were no complaints of pain from participant C during any session. He described the games as innovative and enjoyable. Multiple sensory, visual, proprioceptive, and motor stimuli could potentially distract from the pain by occupying the pathways to the brain. The platform could also provide him a way to realize his old hobbies and improve mental health.

Summary

Overall MMT, pinch, grip strength, and 9-hole peg test all improved after VR plus regular physical therapy. Participants who have a relatively low function (MMT 1-3) may benefit more from VR to improve strength and hand dexterity as compared to those with higher strength. Participants with higher function may still exercise hand dexterity, movement fluidity, motor planning, and movement coordination even though strength training with controllers is relatively light for higher level strengthening.

In this study design, one limitation is we examined VR plus conventional therapy; therefore, we couldn't attribute all improvement to VR intervention alone. We designed the study this way because 1) we believed this is the most practical way to introduce and incorporate VR in the clinic, and 2) as a pilot study we want to test the feasibility in the real world. This study design was also used successfully in the previous studies.[22]

From our feasibility analysis, VR appears to be a safe intervention given there were no adverse events during the study. In the questionnaire, all participants gave high scores to reality level, presence in the virtual world, and engagement in the games. VR was also adaptable to individual participant. As discussed above, each participant had a unique focus in their VR training. Depending on the functional level, interventions can be geared towards UE functional movement, strength and/or pain relief with specific focus as needed.

In order to make this study practical and accessible in clinical settings, we also chose commercially available devices with little modification. The device was easy to access, install and use for clinicians. After the study ended, the subacute rehabilitation center purchased their own VR devices and continues to use them. The game selection through the platform is very broad thanks to a public user base beyond the medical field. We could always find a scenario that fit the participant's preference and functional needs. The evolving platform will keep the participant motivated with new adventures and experiences. We also notice that immersive VR from the market is more entertaining compared to traditional robotics or software which are built for rehabilitation. This means a better reality level, better picture, and more complicated plot. Those factors make it easier to use and enjoy. Participants could find a getaway into a virtual wonderland which could potentially promote mental health especially for those experiencing significant physical limitations. On the other hand, one of the limitations of the game design is laterality. It tends to work different functions in each hand in some games and would result in different training effects in each hand.

Conclusion

This case series suggests that immersive VR with head mount display may be viable to provide safe and effective treatment for patients with SCI who have impaired UE functions though more research needs to be conducted through a larger study. VR training appears to be a possible adjunct to physical and occupational therapy as a method of improving muscle strength, range of motion, fine motor control, bilateral coordination, skill transferability, and improving motivation during subacute rehabilitation. VR demonstrates good adaptability to different needs and levels of function in the clinical setting. Participants with higher level function tend to improve real life performance in terms of speed, coordination and reaction time while lower functional participants demonstrate bigger improvement in muscle strength as well as functional performance. It is feasible for therapists in clinical settings to integrate VR treatment in patient care. Therapists involved in VR treatment are encouraged to leverage on this technology to magnify its therapeutic value and individualize training with each participant.

Chapter Three: Other Clinical Cases

Aside from the three SCI cases in Chapter Two, we also include one participant with traumatic brain injury (BI), acquired brain injury, and chronic cerebrovascular accident (CVA) in this chapter. Their baseline MMSE scores were all 24 and above.

ABI Case

Participant S is a 30 y/o male recruited after acquired brain injury. Following interventions, participant S demonstrated a 7.5-point improvement for MMT composite score, 21 lbs of grip strength improvement for the both hands, 9 lbs of pinch strength improvement for the left and 8 lbs for the right hand. There was clinically meaningful improvement in the 9-hole peg test for bilateral UEs. Participant S presented with spasticity in his UEs and relatively high MMT score at baseline thus VR training without any weight may not have challenged his strength to a therapeutic level. He also commented on the post intervention survey that he thought ROM was most exercised during this intervention. Response time and hand coordination were also challenged in the games added by researchers. He presented with no cognitive deficit; however, motor planning and reaction time were significantly slowed after the acquired brain injury. Improvement in reaction time and hand coordination were evidenced by the clinically meaningful improvement of the 9-hole peg test.

No adverse event occurred throughout the study. It is important to mention participant S was found overdosed in a potential suicidal attempt, so VR was added to his program with the hope to facilitate mental health. He was pleasant and engaged during the study. His top-rated games were Beats Fever, “Ready, Aim, Splat!”, and Fruit Ninja. All of them were competitive games with complex mechanics, especially “Ready, Aim, Splat!”. He had no problem with comprehension despite his brain injury. His family also participated during the intervention. He expressed a high satisfactory score for intervention in the survey.

TBI Case

Participant T is a 42 y/o male recruited after a traumatic brain injury. He demonstrated 3.5 points of total MMT composite score for bilateral UEs. Overall there was no clinically meaningful change in MMT, pinch, grip strength, or 9-hole peg test performance following the interventions. He used a manual wheelchair for mobility and the intensity for strength training may have been too low. He commented that this intervention challenged his eye hand coordination.

Participant T wore glasses and had some fitting issues with the goggles. Goggles are designed to fit everyone even with glasses, however more adjustment is needed for goggles and glasses to align.

Participant T seemed more reserved in session compared to other participants. Family participated in the session several times and provided good feedback. In the survey participant T did rate VR “somewhat more interesting compared to other therapy" and “somewhat enjoyed the training”. It was an interesting observation and could just be attributed to individual personality. There were no adverse events during his sessions.

Chronic CVA case

Participant B is a 56 y/o female recruited 10 months after a chronic stroke with R side impairments. She had finished her course of rehabilitation and was receiving VR-only intervention during the study. Shoulder and finger strength were the targets of the intervention. Based on that rationale, level 4 games with repetitive button and trigger activations were selected to improve fingers strength and coordination. Level 3 games such as Beats Fever were included to improve shoulder strength, endurance, ROM, and speed to movement.

Following the intervention, there was a 7-point increase of total right MMT composite score. Shoulder flexors and abductors were two main contributors to the composite score, increasing from 2- to 3+ for flexors and 4+ for abductors respectively. There was no clinical meaningful change for grip, pinch strength, or 9-hole peg test. Subjectively, she reported the intervention was helpful for reaching and grasping activities and promoted wrist and thumb movement. She also reported the intervention was enjoyable and did not feel like therapy. She also liked that she could visualize her improvement by a score keeping mechanism in the game such as game score, levels and mission completion status.

Participant B was engaged and pleasant during the intervention. She described herself as a passionate gamer. By the end of the study, she inquired about device information for continuing gaming/training at home. No adverse events occurred throughout her participation in the study.

Chapter Four: General Conclusions

1. Clinical decision-making principles

We customized VR training to fit each participant's ability, interest and goals. Here are some general principles we followed to guide and regulate game selection and progression.

Preparation

Candidates receiving VR training will be screened for normal vision or corrected normal vision, no history of epilepsy, and no severe motion sickness before selection. In the first session, participants will be provided with verbal introduction of VR technology. Participants will be asked to park their wheelchair in the designated spot and keep the wheelchair locked once the intervention started. Staff will inform participants to remain seated during the intervention and take breaks as needed. The designated location for the wheelchair is pre-determined by staff, so they can set up the sensors and calibrate the controller in detectable range before the session. Staff will also make sure there is no obstacle within arm-reached distance in any directions. Theoretically no repetitive set-up is needed before each session after the initial set-up, however, it does happen occasionally when there is an issue. In that case, staff will re-connect the goggles first. If not successful, staff will repeat the entire set-up again. When progressed to Level 3 games, Velcro straps could be applied by staff to participants with difficulty holding the controllers.

Selection and Progression

Level 1 is the easiest games among all levels. This level is used to introduce the virtual environment and in the first session. Level 1 game also serves as a quick test of how participants react to VR and if they have any motion sensitivity or elliptical episode before more interactive games. All of our participants could quickly proceed to higher level games after the first run but for participants outside the study population with lower cognitive and functional levels, Level 1 games could be repeated as an intervention. For those participants, Level 1 games will provide environmental stimulus in order to promote consciousness, attention spans, and head and neck control.

For participants with decreased fine motor control in hands, we start them on Level 2 game "Block" with Leap Motion sensor right after Level 1. Leap Motion games work really well with participants in the lower functional levels given the advantages of a tutorial video and a weightless virtual training environment. Participants thus need the ability to follow at least one-step commands in order to follow game tutorial or therapist's instructions in the virtual environment. Participants also need to demonstrate minimum hand function as evidenced by less than 50% of assistance during tutorial activities. Once the participant is able to navigate through the tutorial without cues, therapy staff will create new tasks with higher demands. Tasks include changing shapes of the blocks, using the blocks as "Legos" to build different objects, and performing activities of daily living.

We will progress participants to Level 3 once they demonstrate the ability to hold both controllers with or without assistive strapping. Participants also need to demonstrate endurance for 5 minutes or more in order to complete one repetition of the game. For participants of lower functional levels, "Beats Fever" as an example of Level 3 games will be used to simulate reaching activities. The goal of this level is to achieve functional ROM in upper extremity reaching activities, specifically shoulder and elbow joints which are most practiced in the game. For participants of higher functional levels, this game will be used in the beginning of each session for UE aerobic exercise as a warm-up. Speed, dual-tasking, and motor planning are also exercised depending on the difficulty level in the game. Scores such as A, B, C and D will be given in the game as a general measurement of performance which include components of speed, accuracy, coordination, reaction time and dual tasking ability. Participants are recommended to start from the easiest level and move up one level at a time. We suggest a score higher than "B" to progress to the next level.

For game selection to incorporate simulated hobbies, occupation, goals, and real-life activities driven Level 4 games. This level has the largest library to choose from and allows more flexibility to accommodate more complicated schemes and plots. Staff will explore new games to make sure they are appropriate. Games will be evaluated by story plot, type of virtual environment simulated, requirement for mobility, vision, and cognitive function. See game analysis in Chapter Two for examples. As each simulated activity has its own movement pattern and motor strategy, the decision making in Level 4 games are more case based. Depending on the motor impairment and game complexity, staff need to find the most suitable game that targets the desired motion and muscle groups within the ability of the participant. Generally, participants need to demonstrate finger flexion in order to push buttons, triggers and thumbstick in this level of game. Participants also need to acquire anti-gravity strength in more than half of the major muscle groups in UEs in most cases due to the complexity of the game. The ability to perform different tasks with each limb or each finger is important to participate in this level too. However, there is no set criteria due to the uniqueness in each game. Problem solving and creativity are important to adapt some games into a new play, for example creating new tasks based on the original virtual environment. Staff are encouraged to add therapeutic value to VR by modifying, challenging and progressing motor tasks as in conventional therapy towards the goals of improving performances in recreational or occupational scenarios.

Finally, we put together a flow chart to summarize our clinical decision-making process during game selection and progression as below. Requirements for a lower level game will also apply for the higher-level games.

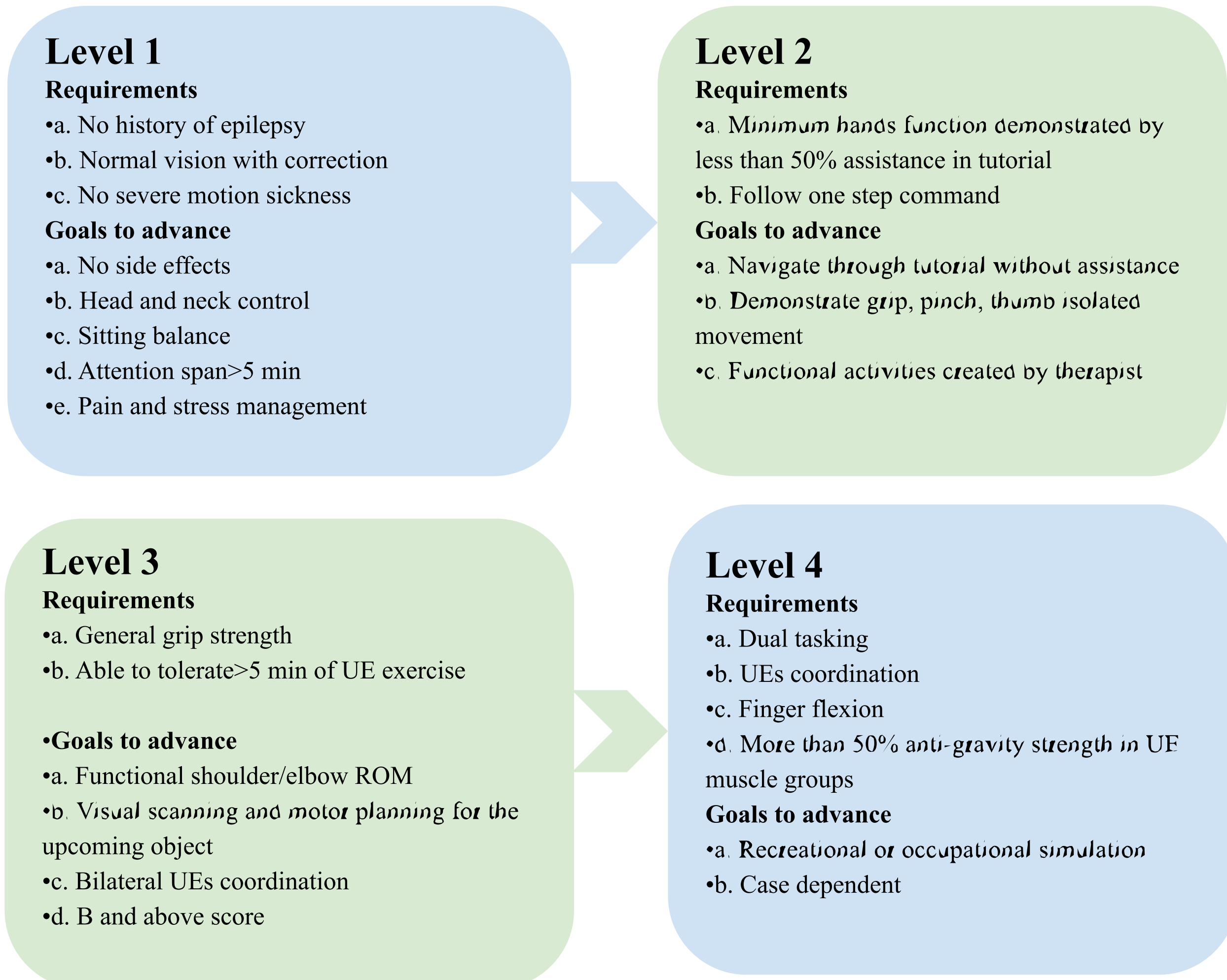

Figure 4: Game selection and progression

2. Limitations and recommendations

1) Study design

In this study, one limitation is that we examined VR plus conventional therapy; therefore, we could not attribute all improvement to VR intervention alone. We designed the study this way because 1) we believed this is the most practical way to introduce and incorporate VR in the clinic, and 2) as a pilot study, we want to test the feasibility in the real world. This study design of VR plus conventional therapy was also used successfully in previous studies.[22] We did not attempt to match or randomize participants to a control group due to the difficulty and bias of matching and randomizing in a small sample pool. However, for future studies with larger sample sizes, it is recommended to include a double-blind control group with conventional therapy only in order to further validate VR efficacy.

2) Games and game console selection

One of the limitations of the VR device is laterality. It tends to work different functions in each hand in some games and would result in different training effects in each hand. This could be an advantage for certain participants in that they highly rely on one hand in training as well as in real life. However, this does reduce the flexibility when we want to work on the non-dominant side. As of now, Oculus device allows you to switch hand dominance in its settings. We would encourage future research teams to discover how hand dominance impacts individual games thus potentially eliminate this limitation.

Another limitation of using non-rehabilitation specific devices like Oculus Rift is the lack of actual weights during higher level weight training. Weightless virtual environment is surely an advantage for low functioning participants to start with; however, as they progress, there is a chance that the pure weight of the controller no longer challenges them. An alternative strategy would be augmented weights at the wrist, elbow or shoulder which we did not explore in this study.

While finding some merits in graphic and plot designs of non-rehabilitation-specific games in our study, we also noticed the increased amount of work for the therapist to match participants with the most appropriate games in terms of intensity, interest, and mobility requirement. Oftentimes it was hard to meet all requirements in one game. There were situations where we found the best real-life stimulation in a game but unfortunately the game required more functional mobility than the participant had. Modifications of the commercially available games is not impossible if they are open sourced. A small change such as slowing down the game flow could dramatically impact the accessibility to a participant with motor deficits; magnifying the movement signal from the participants could increase visual feedback and decrease the difficulty of a game for a lower functioning participant. Due to the scope of our study, we did not modify any game, but the idea of adapting open source VR games to each participant is definitely worth exploring.

3) Outcome measurement

Overall MMT, pinch, grip strength, and 9-hole peg test all improved after VR plus conventional physical therapy. However, as we discussed under each participant, MMT and pinch strength did not well reflect small changes in UE functional strength especially in lower functioning participants. MMT also appeared to be affected by ceiling effects for higher functioning participants. 9-hole peg test was able to capture small functional gains in hand dexterity, however coordination, reaction time, motor planning and dual-task ability in the whole UE are not specifically included in the test. For future studies that compare the statistical significance between groups, it is important to adopt outcome measurements that are holistic, sensitive and standardized for comparison. From an administrative standpoint, researchers should consider time and equipment availability in order to minimize additional work brought to clinicians.

4) Beyond motor function rehabilitation

We gathered a lot of positive feedback from participants. All participants rated VR of high reality and high presence. Two out of the six participants were interested in purchasing the device for home exercise program after discharge. One participant mentioned the enjoyment of fishing again in the simulated environment. One participant who had history of neuropathic pain reported no pain occurred during our training, however, we did not explore further how much VR contributed to his pain management compared to pharmaceutical and conventional therapy. We suggest further study to use standard outcome measurements to monitor and quantify pain and mental status in order to give more insight on the use of VR beyond motor function rehabilitation.

References

1. Deutsch JE, Westcott McCoy S. Virtual reality and serious games in neurorehabilitation of children and adults: prevention, plasticity, and participation. *Pediatr Phys Ther*. 2017;29:S23-S36. doi:10.1097/PEP.0000000000000387

2. de Araújo AVL, Neiva JF de O, Monteiro CB de M, Magalhães FH. Efficacy of virtual reality rehabilitation after spinal cord injury: a systematic review. *BioMed Res Int*. 2019;2019:1-15. doi:10.1155/2019/7106951

3. Yeo E, Chau B, Chi B, Ruckle DE, Ta P. Virtual reality neurorehabilitation for mobility in spinal cord injury: a structured review. *Innov Clin Neurosci*. 2019;16(1-2):13-20.

4. Chinnock C. Virtual reality in surgery and medicine. *Hosp Technol Ser*. 1994;13(18):1-48.

5. Weiss PL, Kizony R, Feintuch U, Katz N. Virtual reality in neurorehabilitation. *Textb Neural Repair Rehabil*. 2006;51(8):182–97.

6. Riva PhD Giuseppe, Davide F. Communications through virtual technologies: identity, community and technology in the communication age. Amsterdam; Washington, DC: IOS Press; 2001. https://trove.nla.gov.au/version/46500245. Accessed April 5, 2019.

7. Gorini A, Gaggioli A, Riva G. Virtual worlds, real healing. *Science*. 2007;318(5856):1549. doi:10.1126/science.318.5856.1549b

8. Deacon BJ, Abramowitz JS. Cognitive and behavioral treatments for anxiety disorders: a review of meta-analytic findings. *J Clin Psychol*. 2004;60(4):429-441. doi:10.1002/jclp.10255

9. Hoffman HG, Richards TL, Coda B, et al. Modulation of thermal pain-related brain activity with virtual reality: evidence from fmri. *Neuroreport*. 2004;15(8):1245-1248.

10. Hoffman HG, Richards TL, Van Oostrom T, et al. The analgesic effects of opioids and immersive virtual reality distraction: evidence from subjective and functional brain imaging assessments. *Anesth Analg*. 2007;105(6):1776-1783, table of contents. doi:10.1213/01.ane.0000270205.45146.db

11. Langhorne P, Bernhardt J, Kwakkel G. Stroke rehabilitation. *Lancet Lond Engl*. 2011;377(9778):1693-1702. doi:10.1016/S0140-6736(11)60325-5

12. Veerbeek JM, van Wegen E, van Peppen R, et al. What is the evidence for physical therapy poststroke? a systematic review and meta-analysis. *PloS One*. 2014;9(2):e87987. doi:10.1371/journal.pone.0087987

13. Lewis GN, Rosie JA. Virtual reality games for movement rehabilitation in neurological conditions: how do we meet the needs and expectations of the users? *Disabil Rehabil*. 2012;34(22):1880-1886. doi:10.3109/09638288.2012.670036

14. Merians AS, Jack D, Boian R, et al. Virtual reality–augmented rehabilitation for patients following stroke. *Phys Ther*. 2002;82(9):898-915. doi:10.1093/ptj/82.9.898

15. Fluet GG, Qiu Q, Patel J, Cronce A, Merians AS, Adamovich SV. Autonomous use of the home virtual rehabilitation system: a feasibility and pilot study. *Games Health J*. 2019;8(6):432-438. doi:10.1089/g4h.2019.0012

16. Villiger M, Liviero J, Awai L, et al. Home-based virtual reality-augmented training improves lower limb muscle strength, balance, and functional mobility following chronic incomplete spinal cord injury. *Front Neurol*. 2017;8:635. doi:10.3389/fneur.2017.00635

17. Patel V, Craig J, Schumacher M, Burns MK, Florescu I, Vinjamuri R. Synergy repetition training versus task repetition training in acquiring new skill. *Front Bioeng Biotechnol*. 2017;5. doi:10.3389/fbioe.2017.00009

18. Massetti T, da Silva TD, Crocetta TB, et al. The clinical utility of virtual reality in neurorehabilitation: a systematic review. *J Cent Nerv Syst Dis*. 2018;10:117957351881354. doi:10.1177/1179573518813541

19. Desrosiers J, Malouin F, Richards C, Bourbonnais D, Rochette A, Bravo G. Comparison of changes in upper and lower extremity impairments and disabilities after stroke. *Int J Rehabil Res*. 2003;26(2):109-116.

20. Pomeroy V, Aglioti SM, Mark VW, et al. Neurological principles and rehabilitation of action disorders: rehabilitation interventions. *Neurorehabil Neural Repair*. 2011;25(5_suppl):33S-43S. doi:10.1177/1545968311410942

21. Stasieńko A, Sarzyńska-Długosz I. Virtual reality in neurorehabilitation. *Adv Rehabil*. 2016;30(4):67-75. doi:10.1515/rehab-2015-0056

22. Yamato TP, Pompeu JE, Pompeu SMAA, Hassett L. Virtual reality for stroke rehabilitation. *Phys Ther*. 2016;96(10):1508-1513. doi:10.2522/ptj.20150539

23. O'Brien HL, Toms EG. What is user engagement? a conceptual framework for defining user engagement with technology. *J Am Soc Inf Sci Technol*. 2008;59(6):938-955. doi:10.1002/asi.20801

24. Ögün MN, Kurul R, Yaşar MF, Turkoglu SA, Avci Ş, Yildiz N. Effect of leap motion-based 3d immersive virtual reality usage on upper extremity function in ischemic stroke patients. *Arq Neuropsiquiatr*. 2019;77(10):681-688. doi:10.1590/0004-282x20190129

25. Wang Z-R, Wang P, Xing L, Mei L-P, Zhao J, Zhang T. Leap motion-based virtual reality training for improving motor functional recovery of upper limbs and neural reorganization in subacute stroke patients. *Neural Regen Res*. 2017;12(11):1823-1831. doi:10.4103/1673-5374.219043

26. Sánchez-Herrera-Baeza P, Cano-de-la-Cuerda R, Oña-Simbaña ED, et al. The impact of a novel immersive virtual reality technology associated with serious games in parkinson's

disease patients on upper limb rehabilitation: a mixed methods intervention study. *Sensors*. 2020;20(8):2168. doi:10.3390/s20082168

27. Laver KE, Lange B, George S, Deutsch JE, Saposnik G, Crotty M. Virtual reality for stroke rehabilitation. Cochrane Stroke Group, ed. *Cochrane Database Syst Rev*. November 2017. doi:10.1002/14651858.CD008349.pub4

28. Jain NB, Ayers GD, Peterson EN, et al. Traumatic spinal cord injury in the united states, 1993-2012. *JAMA*. 2015;313(22):2236. doi:10.1001/jama.2015.6250

29. French B, Thomas LH, Coupe J, et al. Repetitive task training for improving functional ability after stroke. Cochrane Stroke Group, ed. *Cochrane Database Syst Rev*. November 2016. doi:10.1002/14651858.CD006073.pub3

30. Luque-Moreno C, Cano-Bravo F, Kiper P, et al. Reinforced feedback in virtual environment for plantar flexor poststroke spasticity reduction and gait function improvement. *BioMed Res Int*. 2019;2019:1-9. doi:10.1155/2019/6295263

31. Simkins M, Byl N, Kim H, Abrams G, Rosen J. Upper limb bilateral symmetric training with robotic assistance and clinical outcomes for stroke: a pilot study. *Int J Intell Comput Cybern*. 2016;9(1):83-104. doi:10.1108/IJICC-09-2014-0041

32. Browning MHEM, Mimnaugh KJ, van Riper CJ, Laurent HK, LaValle SM. Can simulated nature support mental health? comparing short, single-doses of 360-degree nature videos in virtual reality with the outdoors. *Front Psychol*. 2020;10:2667. doi:10.3389/fpsyg.2019.02667

33. Khurana M, Walia S, Noohu MM. Study on the effectiveness of virtual reality game-based training on balance and functional performance in individuals with paraplegia. *Top Spinal Cord Inj Rehabil*. 2017;23(3):263-270. doi:10.1310/sci16-00003

34. Saposnik G, Cohen LG, Mamdani M, et al. Efficacy and safety of non-immersive virtual reality exercising in stroke rehabilitation (evrest): a randomised, multicentre, single-blind, controlled trial. *Lancet Neurol*. 2016;15(10):1019-1027. doi:10.1016/S1474-4422(16)30121-1

35. Bohannon RW. Minimal clinically important difference for grip strength: a systematic review. *J Phys Ther Sci*. 2019;31(1):75-78. doi:10.1589/jpts.31.75

36. Oxford Grice K, Vogel KA, Le V, Mitchell A, Muniz S, Vollmer MA. Adult norms for a commercially available 9-hole peg test for finger dexterity. *Am J Occup Ther*. 2003;57(5):570-573. doi:10.5014/ajot.57.5.570

37. Chen H-M, Chen CC, Hsueh I-P, Huang S-L, Hsieh C-L. Test-retest reproducibility and smallest real difference of 5 hand function tests in patients with stroke. *Neurorehabil Neural Repair*. 2009;23(5):435-440. doi:10.1177/1545968308331146

38. Dick JP, Guiloff RJ, Stewart A, et al. Mini-mental state examination in neurological patients. *J Neurol Neurosurg Psychiatry*. 1984;47(5):496-499. doi:10.1136/jnnp.47.5.496

39. Tombaugh TN, McIntyre NJ. The mini-mental state examination: a comprehensive review. *J Am Geriatr Soc*. 1992;40(9):922-935. doi:10.1111/j.1532-5415.1992.tb01992.x

Appendix A: Questionnaire

Section one --About the presence

1. In the computer-generated world, I had a sense of "being there"
    a. Extremely
    b. Very
    c. Moderately
    d. Slightly
    e. Not at all

2. Somehow, I felt that the virtual world surrounded me.
    a. Strongly agree
    b. Agree
    c. Undecided
    d. Disagree
    e. Strongly disagree

3. I felt like I was just perceiving pictures.
    a. Strongly agree
    b. Agree
    c. Undecided
    d. Disagree
    e. Strongly disagree

4. I did not feel present in the virtual space.
    a. Did not feel
    b. Felt present

5. I had a sense of acting in the virtual space, rather than operating something from outside.
    a. Strongly agree
    b. Agree
    c. Undecided
    d. Disagree
    e. Strongly disagree

6. I felt present in the virtual space.
    a. Strongly agree
    b. Agree
    c. Undecided
    d. Disagree
    e. Strongly disagree

7. How aware were you of the real world surrounding while navigating in the virtual world? (i.e.

sounds, room temperature, other people, etc.)?
   a. Extremely aware
   b. Very aware
   c. Moderately aware
   d. Slightly aware
   e. Not at all

8. I was not aware of my real environment.
   a. Strongly agree
   b. Agree
   c. Undecided
   d. Disagree
   e. Strongly disagree

9. I still paid attention to the real environment.
   a. Strongly agree
   b. Agree
   c. Undecided
   d. Disagree
   e. Strongly disagree

10. I was completely captivated by the virtual world.
   a. Strongly agree
   b. Agree
   c. Undecided
   d. Disagree
   e. Strongly disagree

11. How real did the virtual world seem to you?
   a. Completely real
   b. Very real
   c. Moderately real
   d. Slightly real
   e. Not real at all

12. How much did your experience in the virtual environment seem consistent with your real-world experience?
   a. Not consistent at all
   b. Slightly consistent
   c. Moderately consistent
   d. Very consistent
   e. Extremely consistent

13. How real did the virtual world seem to you?
   a. About as real as an imagined world
   b. Indistinguishable from the real world

14. The virtual world seemed more realistic than the real world.
    a. Strongly agree
    b. Agree
    c. Undecided
    d. Disagree
    e. Strongly disagree

Section two—About satisfactions in the training

1. Do you enjoy the virtual reality invention in general?
    a. Very enjoy
    b. Somewhat enjoy
    c. Neither
    d. Somewhat don't like it.
    e. Very against it

2. Do you think VR training is more interesting than other trainings?
    a. Much better
    b. Somewhat better
    c. Stayed the same
    d. Somewhat worse
    e. Much worse

3. Do you think VR training is helpful in the term of training outcomes?
    a. Yes, it helped a lot
    b. Yes, it helped a bit
    c. Can't tell
    d. No, no improvement
    e. No, got worse

4. I feel it is easier to finish the task without real gravity like in the VR games.
    a. Strongly disagree
    b. Disagree
    c. Neither
    d. Agree
    e. Strongly agree

5. Overall, how satisfied or dissatisfied are you with the VR training?
    a. Very satisfied.
    b. Somewhat satisfied.
    c. Neither satisfied nor dissatisfied.
    d. Somewhat dissatisfied.
    e. Very dissatisfied.

Section three----About improvement of the training

1. Did the therapist give you the proper instructions?
   a. Yes, just fine.
   b. Fine, but hope there's more.
   c. Fine, but hope there's less.
   d. No, it's too much.
   e. No, it's too few.

2. Do you think proper assistance from the therapist is necessary?
   a. Yes, very much.
   b. Yes, somewhat necessary.
   c. Neutral
   d. No, somewhat unnecessary.
   e. No, not at all.

3. Do you need time to get used to this new invention?
   a. No.
   b. Yes, after 5 times
   c. Yes, after 15 times.
   d. Yes, after 30 times.
   e. Never get used to it.

4. Did you play any of the VR or related games before?
   a. Yes.
   b. No.

5. Do you find some difficulties in VR training?
   a. Yes, a lot of difficulties.
   b. Yes, moderate challenging and helpful.
   c. Yes, only a few.
   d. No, not at all.

6. Please describe in a few words of your overall experience, comments or suggestions.

   ____

Appendix B: Consent form

ADULT CONSENT - CLINICAL BIOMEDICAL

Invitation

You are invited to take part in this research study. You have a copy of the following, which is meant to help you decide whether or not to take part:

Informed consent form
"What Do I need to Know Before Being in a Research Study?" The Rights of Research Subjects

Why are you being asked to be in this research study?

You are being asked to be in this study because you had one of the three neurological disorders: stroke, spinal cord injury, or traumatic brain injury within the last 12 months and your upper arm function has not been fully recovered. You do not have trouble following instructions and can communicate with others. You have a normal or corrected normal vision and you have no history of seizure disorder. If you are pregnant, or plan to become pregnant during this study, you may not be in this study.

What is the reason for doing this research study?

The purpose of the study is to evaluate a commercially available virtual reality equipment as an intervention for upper arm rehabilitation among stroke patients, spinal cord injury patients or traumatic brain injury patients. The software used for the training is from Leap Motion Inc., a company that manufactures software designed for hand tracking in virtual reality.

What will be done during this research study?

Should you agree to participate in this study, you will be asked to complete the Mini-Mental Status Exam to demonstrate your ability to follow instructions during the study. You will be also asked to complete a set of exams including Manual muscle testing, pinch and grip strength testing and other functional assessments to determine if you are eligible for this study and also keep as the original data before intervention.

Then you will be assigned a weekly training program that includes either virtual reality games plus conventional therapies or conventional therapies only in a total of 3-5 sessions a week and 45 minutes each session during a six-month period of your stay in QLI. You will be followed up in 1-month and 3-month by phone at the next primary care clinics, to report muscle strength of upper limb extremity and upper limb function. Each telephone visit will last about 20 minutes.

In the virtual reality training session, you will be seated in front of a computer and given enough space for arm movements under the supervision of your therapist. You will wear a pair of goggles which generate a virtual environment in front of you and the sensor on the goggles will capture your hands and arms movements and interactively present your movements in the virtual word. Tasks, such as moving virtual objects, pinching virtual candles, will be given.

After the first training you be asked to fill out a questionnaire either on your own or with the help from your therapist. Questions involve the sense of presence in the virtual reality game, enjoyment, difficulties, and concerns surrounding virtual reality training. The same questionnaire will be given to you to fill at the end of the whole training program.

Conventional therapy:

The conventional therapies such as fine motor training/coordination, and functional grip strength training will be practiced at QLI.

Assessments include muscle strength test, grip strength test, pinch strength test, coordination test will be performed every other week during the period of staying at QLI.

What are the possible risks of being in this research study?

It is possible that you might have eye strain, dizziness, nausea and motion sickness; however, these effects are believed to be temporary with no lasting effect. Potential risks of this study are not expected to be any greater than performing normal physical activity, for example, muscle soreness following exercise.

If you feel uncomfortable, you can rest as often as you wish and then continue the exercise, or you can stop at any time if you really cannot go any further. It is possible that other rare side effects could occur which are not described in this consent form. It is also possible that you could have side effects that have not occurred before.

What are the possible benefits to you?

You may not receive any benefit by participating in this study. However, you might benefit from being in this study because you may understand your current functional status. You may also improve your upper arm functions after training.

What are the possible benefits to other people?

Your participation in this study may help us to have better evaluations utilizing virtual reality games in upper extremity rehabilitation. This may allow us to better train more people using virtual reality to potentially improve pinch strength, grip strength, coordination and overall upper arm function in patients undergoing upper extremity rehabilitation.

What are the alternatives to being in this research study?

Instead of being in this research study, you can choose not to participate.

What will being in this research study cost you?

There is no cost to you to be in this research study.

Will you be paid for being in this research study?

You will not be paid to be in this research study.

Who is paying for this research?

This research is being paid for by the Department of Physical Therapy Education of the University of Nebraska Medical Center (UNMC).

What should you do if you are injured or have a medical problem during this research study?

Your welfare is the main concern of every member of the research team. If you are injured or have a medical problem or some other kind of problem as a direct result of being in this study, you should immediately contact one of the people listed at the end of this consent form.

How will information about you be protected?

You have rights regarding the protection and privacy of your medical information collected before and during this research. This medical information is called "protected health information" (PHI). PHI used in this study may include your medical record number, address, birth date, medical history, the results of physical exams, blood tests, x-rays as well as the results of other diagnostic medical or research procedures. Only the minimum amount of PHI will be collected for this research. Your research and medical records will be maintained in a secure manner.

Who will have access to information about you?

By signing this consent form, you are allowing the research team to have access to your PHI. The research team includes the investigators listed on this consent form and other personnel involved in this specific study at UNMC.

Your PHI will be used only for the purpose(s) described in the section "What is the reason for doing this research study?"

You are also allowing the research team to share your PHI, as necessary, with other people or groups listed below:

- The UNMC Institutional Review Board (IRB)
- Institutional officials designated by the UNMC IRB
- Federal law requires that your information may be shared with these groups:
    - The HHS Office for Human Research Protections (OHRP)

You are authorizing us to use and disclose your PHI for as long as the research study is being conducted. You may cancel your authorization for further collection of PHI for use in this research at any time by contacting the principal investigator in writing. However, the PHI which is included in the research data obtained to date may still be used. If you cancel this authorization, you will no longer be able to participate in this research.

How will results of the research be made available to you during and after the study is finished?
In most cases, the results of the research can be made available to you when the study is completed, and all the results are analyzed by the investigator or the sponsor of the research. The information from this study may be published in scientific journals or presented at scientific meetings, but your identity will be kept strictly confidential.

If you want the results of the study, contact the Principal Investigator at the phone number given at the end of this form or by writing to the Principal Investigator at the following address: 894420 Nebraska Medical Center, Omaha, NE, 68198

What will happen if you decide not to be in this research study?

You can decide not to be in this research study. Deciding not to be in this research will not affect your medical care or your relationship with the investigator or UNMC. Your doctor will still take care of you and you will not lose any benefits to which you are entitled.

What will happen if you decide to stop participating once you start?

You can stop participating in this research (withdraw) at any time by contacting the Principal Investigator or any of the research staff. Deciding to withdraw will otherwise not affect your care or your relationship with the investigator or UNMC. You will not lose any benefits to which you are entitled.

For your safety, please talk to the research team before you stop taking any study drugs or stop other related procedures. They will advise you how to withdraw safely. If you withdraw you may be asked to undergo some additional tests. You do NOT have to agree to do these tests.

Any research data obtained to date may still be used in the research.

Will you be given any important information during the study?

You will be informed promptly if the research team gets any new information during this research study that may affect whether you would want to continue being in the study.

What should you do if you have any questions about the study?

You have been given a copy of "*What Do I Need to Know Before Being in a Research Study?*" If you have any questions at any time about this study, you should contact the Principal Investigator or any of the study personnel listed on this consent form or any other documents that you have been given.

What are your rights as a research participant?

You have rights as a research subject. These rights have been explained in this consent form and in The Rights of Research Subjects that you have been given. If you have any questions concerning your rights, or want to discuss problems, concerns, obtain information or offer input, or make a complaint about the research, you can contact any of the following:

- The investigator or other study personnel
- Institutional Review Board (IRB)
    - Telephone: (402) 559-6463
    - Email: IRBORA@unmc.edu
    - Mail: UNMC Institutional Review Board, 987830 Nebraska Medical Center, Omaha, NE 68198-7830
- Research Subject Advocate
    - Telephone: (402) 559-6941
    - Email: unmcrsa@unmc.edu

Documentation of informed consent

You are freely making a decision whether to be in this research study. Signing this form means that:

- You have read and understood this consent form.
- You have had the consent form explained to you.
- You have been given a copy of The Rights of Research Subjects
- You have had your questions answered.

- You have decided to be in the research study.
- If you have any questions during the study, you have been directed to talk to one of the investigators listed below on this consent form.
- You will be given a signed and dated copy of this consent form to keep.

Signature of Subject ___________________________ Date ___________

My signature certifies that all the elements of informed consent described on this consent form have been explained fully to the subject. In my judgment, the subject possesses the legal capacity to give informed consent to participate in this research and is voluntarily and knowingly giving informed consent to participate.

Signature of Person obtaining consent ___________________________ Date ___________

Authorized Study Personnel Principal
* Zhang, Anqi
alt #: 402-238-9291 degree: BS

Secondary

* Dexter, Bradley phone: 402-573-3759 alt #: 402-554-3811 degree: DPT

* Volkman, Kathleen phone: 402-559-5014 alt #: 402-559-6415 degree: PT, MS

* McNamara, Erin degree: OT

Faculty Advisor

Siu, Ka-Chun (Joseph) phone: 402-559-8464 alt #: 402-559-8464 degree: PhD