IRB Protocol

Study Title:

Effect of Constraint-Induced Gaming Therapy in an Acute Care Setting

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Background and Significance

Stroke represents a national health concern given approximately 800,000 cases annually.[29] This number is increasing given shifting demographics due to most baby-boomers reaching retirement age. Providers of care to veterans in the Veterans Health Administration (VHA) see approximately 6,000 cases of ischemic stroke annually. This results in a growing care population that receives ongoing treatment within the VA system. The cost of care to a stroke survivor is noted to be more than three times that of the average veteran patient.[30] Improved treatment regimens are essential for reducing losses in quality of life for veterans and their families and in reducing the cost of long-term care.

Significant reform in the way that post-stroke care is delivered is needed. The standard for most inpatient rehabilitation facilities is 3 hours per day spent engaging in one-on-one therapeutic interventions with a therapist. Not only is this approach costly, but new literature partially erodes empirical support for this policy.[31] A more distributed training approach involving frequent mobilization for shorter periods was associated with better health and function. Conversely more total hours spent in therapy had the opposite effect.[7,8] Preference for distributed training is consistent with patient perspectives on the necessity of adequate rest during early rehabilitation and animal literature showing that very early intense motor training can be associated with deleterious effects on brain structure and motor function.[32-34] Studies also suggest that there may be a critical time window of heightened neuroplasticity within the first few weeks post-stroke that may be bypassed if training does not emphasize neurorestoration (e.g., focuses exclusively on compensatory techniques)[35-40] and that increasing complex motor activity enhances neurorestoration.[41-47] Taken together, this literature indicates that frequent short-lived practice with the more affected upper extremity may convey the optimal benefit. Current care does not meet this standard well given that patients remain sedentary for much of the day[48,49] and have limited opportunities for activity outside of therapy hours. The recommended distributed training approach cannot be easily employed within existing face-to-face treatment models of care due to staffing schedules (therapist tour 7:30-4 on weekdays) and increased documentation burden with distributed face-to-face treatment with a therapist. A potential solution to this problem is to supplement therapist care with technologies that can be utilized independently by patients during idle times of the day.

Another problem with inpatient rehabilitation planning is the paucity of definitive clinical trials to inform the type of motor practice that should be administered. Constraint-Induced Movement (CI) therapy is arguably the most empirically-supported upper extremity intervention in subacute and chronic stroke, with strong evidence of increased effectiveness relative to standard care from the only positive definitively-powered upper extremity trial.[15,16] Emerging evidence suggests that this is due to CI therapy being the only motor intervention to incorporate behavioral techniques designed to promote carry-over of training from practiced exercises to daily activities.[23,24,26] These Transfer Package techniques include contracting, daily self-assessment of arm use, and problem-solving. Compared to other high-intensity dose-matched interventions that do not increase arm use for daily activities,[25] CI therapy combats learned nonuse, which translates into maintenance of therapeutic gains over time.[50,51] Given that extent of carry-over of motor training to daily activities is strongly associated with improved quality of life (but extent of motor improvement is not),[28] the carry-over techniques of CI therapy appear essential to optimal treatment success. The effects of these carry-over techniques in acute stroke have not been well established, however. With the exception of one study,[52] all studies on acute CI therapy to date [17-22] omitted the behavioral strategies that promote carry-over of training, arguably the most essential components of CI therapy. Patient-centered research that seeks to adapt the CI therapy carry-over techniques to the inpatient rehabilitation setting is needed to foster increased acceptance and use of this approach.

Finally, there is the problem of inadequate and disparate continuity of care post-discharge,[53,54] that particularly adversely impacts rural dwellers and other underserved communities.[55] Accordingly, function typically declines post-discharge (rather than continues to improve when intensive rehabilitation is available).[12,13]

Amongst CI therapy trials, the treatment advantage of CI therapy relative to standard care also declines post-discharge.[7] This may be due to lack of continuity of treatment during a chaotic time in patientsâ€™ lives when they are placed into either understaffed nursing facilities or return home to families that are ill equipped to provide the enriched therapeutic environment that promotes neurorestoration.[41-44] Alternatively or in addition, limited use of the CI therapy behavioral techniques designed to promote carry-over of training to daily activities may have adversely affected retention. A potential solution to the backslide in function/wellness that occurs post-discharge is portable treatment technology introduced acutely that could seamlessly continue throughout the subacute and chronic phases of treatment.

Preliminary Studies

A potential solution to the aforementioned problems is to integrate existing face-to-face care with portable video-game technology that incorporates the principles of CI therapy. The ideal patient-centered approach to CI therapy would seemingly begin within the acute setting to discourage non-use, maximize opportunities for training throughout the day, allow for more distributed practice in shorter intervals, integrate behavioral strategies to promote carry-over of training to daily activities, and continue post-discharge to maintain the CI therapy treatment advantage.[7]

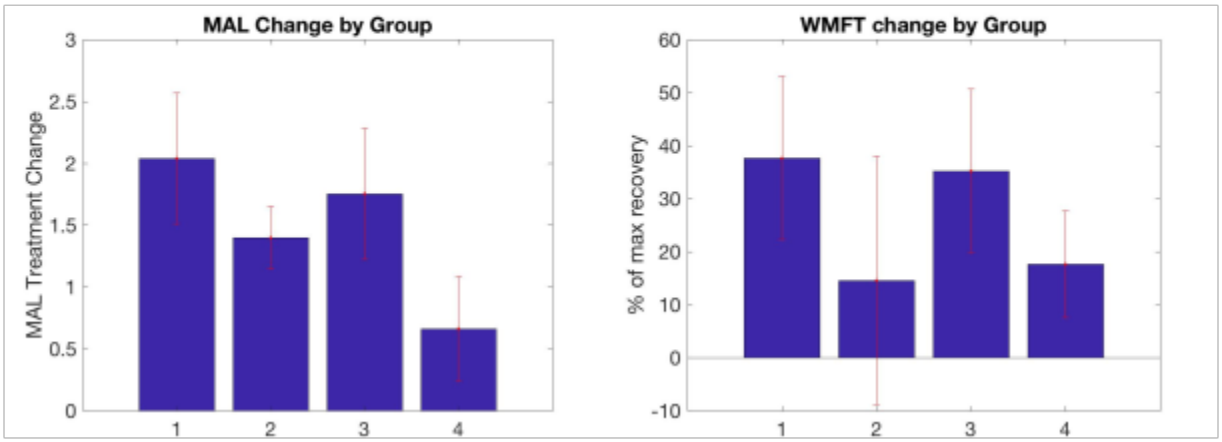
Collaborator Gauthierâ€™s research team at Ohio State University, in conjunction with patient stakeholders, created a video-game-based CI therapy delivery system that has promise to address some of the barriers (Figure 1). This system, named Recovery Rapids, involves self-paced independent game play between periodic consultations with a therapist. Recovery Rapids serves as an engaging virtual therapist, automatically progressing the difficulty of in-game motor demands to a userâ€™s current ability level.[56,57] As the game is played independently at a personâ€™s own pace outside of therapy sessions throughout the day (frequent mobilization), therapists are now able to devote substantial time to promoting carry-over to activities of daily living. Carry-over is also promoted outside of therapy sessions through a smart-watch biofeedback app that prompts movement when prolonged periods of inactivity are detected (this app replaced the CI therapy restraint-mitt that was not well tolerated by patients).

Figure 1 – Recovery Rapids gaming system.

Amongst community dwelling individuals with chronic stroke (ongoing multi-site RCT[76]), patient satisfaction with the intervention was high.[58] Moreover, this system appears superior to standard physiotherapy and is roughly equivalent to in-clinic CI therapy at improving both motor function and

daily arm use (Figure 2), at only a small fraction (<25%) of the cost. The feasibility and efficacy of implementing this low-cost treatment model in an acute care setting has yet to be established, however.

Figure 2: Comparative effectiveness of game-based CI therapy (Grp 3) versus traditional CI therapy (Grp 1) and standard physiotherapy (Grp 4) in an ongoing multi-site RCT (n=41). WMFT=Wolf Motor Function Test; MAL = Motor Activity Log.



Research Design and Methods

The first 3 months of the project will involve participatory action research methods to identify potential barriers to implementation of this new intervention within the VA and to refine the treatment approach to meet the needs of an inpatient population. A half-day focus group â€œretreatâ€ will involve at least 3 patients who are currently on the inpatient rehabilitation unit (or recently discharged), their families, and OT/PT/recreational therapy staff. This meeting will serve to finalize the treatment protocol for this study. Areas that will be addressed will include the â€œdosingâ€ schedule for the game-based intervention and needed adaptations to the CI therapy Transfer Package techniques (described below) to promote maximal carry-over from trained activities to everyday use of the weaker upper extremity. Any needed modifications to the technology platform (e.g. data storage) will also be made to comply with the VAâ€™s regulatory policies regarding adoption of new technology.

Setting of Research Study

This study will be conducted at the Minneapolis Veterans Affairs Medical Center (MVAMC). The MVAMC is home to the Stroke Specialty Program (SSP), a CARF accredited program. The SSP tailors rehabilitation for survivors of any stroke mechanism (hemorrhagic, occlusive, etc.) affecting any part of the brain. Services can be adapted for survivors with cognitive challenges. The SSP has averaged 41 admissions in the past three years, though 2017 has projected admissions over 50. Retrospective chart review demonstrates the primary diagnosis resulting from stroke to be hemiplegia in approximately half of the admissions. Most patients (85%) are older than 60 years, predominantly Caucasian (85%) or African-American (10%) and male (98%).

Recruitment: Prospective participants will be screened by a clinician. Patients meeting study criteria will begin the consenting process. We will attempt to recruit twelve subjects each year for a sample of 24. Assuming 20% attrition by 3-month follow-up, we anticipate a sample of 20.

Game-based CI therapy participants will have access to Recovery Rapids and the smart-watch biofeedback app both on the unit and post-discharge and will be exposed to Transfer Package techniques. Recovery Rapids was developed in collaboration with stakeholders and utilizes inexpensive and commercially available gaming/sensor technology (Microsoft Kinectv2) to provide rehabilitation to individuals in their own homes. The Kinect-based game requires users to trigger game actions by performing intuitive movements (gestures) that are characteristic of real-life motor demands.[56,57] As such, gestures are typically complex and involve both proximal and distal movement (e.g., shoulder flexion with elbow extension and supination). Proximal movements include shoulder flexion/abduction/ adduction and elbow flexion/extension. Distal movements include those that can be reliably detected by the Kinect: forearm supination, grasp/release, and wrist extension. The user utilizes various gestures to paddle a kayak through a river canyon (Fig 1), while collecting hidden treasure, fishing for food, capturing essential supplies that are parachuted down from above, gathering food, solving puzzles, and pulling objects from the river. Bats can attack, river rapids can crash the kayak into the rocks, and low hanging obstacles need to be avoided. To promote adequate dosing, the game utilizes procedural content generation to generate infinite novel content. This game-based rehabilitation incorporates elements of constraint-induced movement (CI) therapy, including shaping (progressively increasing the difficulty of required motor movements as a patient obtains mastery) and rapid customizability to the preferences/needs of the therapist and client. To accomplish shaping, a gesture library for each of the 10 possible complex movements consists of multiple difficulty levels, each progressing in the range of motion that must be exerted at a particular joint to trigger the desired game mechanic. More complex gestures have up to 25 different levels of difficulty. The gaming technology to be employed here â€œlearnsâ€ what the user is capable of and self-calibrates the difficulty of the movements to the clientâ€™s level of ability within 30 minutes of therapist-supervised game play. This means that it will no longer respond to poorer movement mechanics than the user is capable of. This means that when a client engages in unsupervised practice, the game will only respond to movements executed according to the movement mechanics that a therapist taught in-session, implicitly preventing weaker attempts. The game also continues to update these difficulty settings as a user displays improvement.

Participants will begin playing the Recovery Rapids game when clinically appropriate per the clinician, at least 1 week prior to discharge. We anticipate at least three sessions with an OT will be devoted to teaching the game and personalizing game play to the individual. Though the exact dosing schedule will be refined based on stakeholder feedback gathered during preparatory work, game play will then occur independently outside of OT/PT sessions. Study clinicians will determine how often participants should engage in the game, with a general recommendation being 10-minute periods three times per day with the possibility for more gameplay on weekends. Recreation therapy staff will assist participants with game setup as needed. Participants will be asked to track how much time they spend on the game. Study clinicians will engage in adherence strategies that are typically used clinically with the participant to enhance use of the gaming system as needed.

Participants will have the option of wearing smartwatches (Figure 3) on both upper extremities targeting a wearing schedule of: all waking hours during the inpatient stay and 3-month follow-up. An app on the smart-watch uses accelerometer hardware to record the number of movements performed. The app also enables notifications (vibration coupled with â€œPlease use meâ€ text prompt) if the arm is not utilized for a period of 10 minutes. Notification will be set to â€œonâ€ for the weaker arm and â€œoffâ€ for the stronger arm.

Figure 3: Smart-watch Biofeedback device.

Participants will also receive the CI therapy Transfer Package techniques. These include contracting (â€œbuy-inâ€ to utilize the more affected arm for as many daily tasks as possible), daily self-assessment of use of the weaker arm, guided problem solving to overcome barriers to using the weaker arm, and deliberate practice with the more affected upper extremity for activities of daily living.23,24 Thirty minutes of occupational therapy 3 times per week, or as needed, will be allocated to transfer package techniques. After they are discharged, participants will have the option to take the game home with them and continue with gameplay for 3 months. At the three-month follow-up, participants will bring the gaming system back to the VA for data retrieval using a VA issued Iron Key. The systems will only be turned on in research-designated spaces and will not be reused between Veterans, which is in line with Sterile Processing Services policy. CI therapy participants will assume ownership of the gaming system post-discharge. This will facilitate continuing therapy during transition home.

During OT sessions not containing gameplay or the Transfer Package, participants will engage in standard occupational therapy. Standard occupational therapy intervention options for inpatient stroke rehab patients with UE neuromotor impairments include active assisted range of motion exercise, morning bedside ADL sessions, high-repetition task-specific training, mirror therapy, Digi-flex, theraputty, TheraBand, free weights, weighted therapy bars for strengthening exercises in clinic and use with home exercise programs (HEP). Additional tools used as determined by therapist include FES modalities to assist with upper extremity neuromotor re-education, unweighted reaching tasks via the ArmeoSpring, and functional work task training/strengthening. They also participate in recreation therapy as appropriate. A log of occupational therapy intervention options used will be maintained for all participants in both groups to facilitate retrospective analysis of data.

Table 1: Gaming CI Therapy Interventions

Gaming CI Therapy
1) Approximately 30 total inpatient hours OT/PT: • 3+ 30 min sessions to teach game play • Approximately 4.5 hours devoted to Transfer Package • Remainder time spent in usual care activities 2) 10.5 hours independent game play is encouraged while inpatient 3) 18 hours independent game play is encouraged following discharge (30 min, 3 times weekly) over and above standard care (will be documented as covariate) 4) Use of smart watch with biofeedback

Retrospective Chart Review: We will conduct a chart review of Veterans who have participated in inpatient stroke rehabilitation at the Minneapolis VA over the past 5 years. Veterans whose charts will be reviewed will be identified by clinician members of the study team. We will review the medical records of each Veteran using CPRS and extract the relevant data. This will include demographic data (e.g. age, diagnosis, location, etc.), clinical data (e.g. outcome measures, interventions provided) and may include other clinical information as needed to adequately describe our sample. Data pulled from Veteran charts will be used as a retrospective control for the participants who receive the study intervention.

Approach to Aim 1: Determine the extent to which game-based CI therapy increases use of the more affected upper extremity from inpatient rehabilitation through subacute follow-up. For participants who use the smartwatch app, arm use will be tracked via a smart-watch app (see above) during the inpatient stay and post-discharge. Smart-watch biofeedback notifications for the standard care group will be set to â€œonâ€ for the weaker arm and â€œoffâ€ for the stronger arm. Missing data (e.g., participant forgot to put the watch on one day) will be interpolated from data obtained during compliant days. The primary repeated-measures outcome will be total movement counts for each 1-week epoch from baseline through 3 months post-discharge (~12 weeks).

Approach to Aim 2. Pilot the clinical effectiveness and feasibility of distributed gaming CI therapy for improving motor function of the more affected upper extremity at 3 months post-discharge. Motor function will be assessed prior to treatment, before discharge, and at 3 monthsâ€™ follow-up by an OT. The primary outcome will be improvement on the Action Research Arm Test at post-treatment. The ARAT measures the time to complete standardized UE movements, with established reliability and validity. [60-63] Secondary measures of impairment, quality of life, and satisfaction with the gaming system may include the Wolf Motor Function Test (WMFT), Fugl-Meyer [64-67], Neuro-QoL[68-70], and the Quebec User Evaluation of Satisfaction with assistive Technology (QUEST) respectively.

Statistical Analysis: Statistical analysis will be jointly led by our off-site collaborator Lynne Gauthier and the VA biostatistician. We plan to compare therapy induced changes in motor function (ARAT) and potentially motor impairment (Fugl Meyer) , UE function (WMFT), and quality of life (Neuro-QoL) via mixed effects linear models or non-parametric equivalents will be used. We plan to examine outcome measure scores over time using graphical means. Statistical testing will be used to determine whether individuals lost to follow-up differ from those who completed the study.

Timeline: Institutional Review Board (IRB) review will be completed after funding is confirmed and before receipt of funding. Two-four patients per quarter will be recruited, with recruitment completing by month 19. The next 3 months will involve final follow-up data collection. The final 3 months will involve data analysis and publication preparation.

Table 2. Proposed Project Timeline

Effect of Constraint-Induced Gaming Therapy in an Acute Care Setting	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
Participatory Action Research Methods								
Identify Ideal Implementation of Gaming CI Therapy								
Work with Tech Transfer								
Data Acquisition & Follow-up								
Data Processing and Analysis								
Annual and final reports to VA RR&D Service								
Dissemination of knowledge gained during the project								

Justification for pilot work: The proposed work represents a new approach to inpatient rehabilitation utilizing new gaming and biofeedback technology that has not yet been tested in this setting. To our knowledge, this will represent the first inpatient study whose focus is empirically-based CI therapy with distributed dosing and continuity of care post-discharge. Initial evidence of effectiveness of this new approach needs to be established prior to initiating a definitive trial given (1) very limited evidence exists to support or refute the use of CI therapy in inpatient rehabilitation, (2) a critical component of CI therapy was omitted in prior work, and (3) needed modifications to the CI therapy Transfer Package have yet to be established.

Future work: The proposed work will establish the initial efficacy and feasibility of implementing the proposed model of care in an inpatient setting. It will also ensure that use of the gaming and biofeedback technology can be seamlessly integrated into future work within the VA system. Future work through a VA R&D Merit Review or PCORI grant will definitively examine the comparative effectiveness of this approach, incorporate a longer follow-up period, and include cost-effectiveness measurement. The end result of this research program would be definitive evidence that could transform rehabilitation policy, lower costs, and enhance the way that inpatient rehabilitation care is delivered.

Relevance to the VA mission: Access to post-discharge care is limited and largely dependent on geography and availability of transportation (e.g., veterans in rural areas often lack access).[55] Although post-stroke motor disability is typically a chronic condition, the current health care model provides relatively short episodes of care. Accordingly, function typically declines post-discharge.[12] Home-based treatment has been shown to reduce this trend at lower cost than in-clinic treatment.[71] In-home gaming treatment may improve care through continued unlimited access to motor rehabilitation, while further reducing costs.

The ability of this home-based model to revolutionize care delivery likely hinges on the extent to which it can be integrated into the inpatient setting. By initiating game-based treatment during the inpatient rehabilitation stay, patients and caregivers can become comfortable with the technology before they return home. Patients and families have told us that this exposure is essential, as they are often too overwhelmed during the transition-to-home period to pursue new approaches. In addition, inpatient staff that had not delivered a gaming intervention did not refer eligible individuals to a home-based gaming rehabilitation research program, despite weekly outreach by research staff.[72] Qualitative data from patients indicating that they would be unlikely to seek new alternatives upon returning home and evidence of poor referral rates to a home-based gaming program suggests that a strong pipeline between inpatient and outpatient care is needed for adoption/penetration of tech-based approaches.

Discharging patients with the gaming system that they utilized during their inpatient stay would enable immediate access to unlimited rehabilitation upon returning home, reduce care disparities and likely reduce long-term care costs.[73] Moreover, the gaming system would already be optimally customized to each clientâ€™s level of ability upon first in-home use. The proposed pipeline from inpatient to community treatment will therefore enable high-repetition in-home practice to therapist specification without requiring continued access to a therapist. It thus has the potential to improve outcomes and reduce care disparities. It may also help prevent secondary health complications (e.g., deconditioning, weight gain, frozen shoulder)[77] by encouraging increased mobilization post-discharge.

Lastly, this project responds to calls for greater access to care by improving the continuity of care for patients who incur stroke by extending active intervention from the acute phase of treatment through discharge and into home-based therapy. This model of care has the promise to improve long-term outcomes, increase quality of life and reduce cost of ongoing care.

1. Risks to Subjects

Human Subjects Involvement and Characteristics.

For Community Based Participatory Model, study participants (least 3 patients who are currently on the inpatient rehabilitation unit or recently discharged, their families, and OT/PT/recreational therapy staff) will offer suggestions and feedback related to design of a video game-based rehabilitation program. Their opinions may be recorded via audio recording and/or video recording. Audio/video recordings will be kept confidential. This may involve a focus group discussion or one-to-one interview. Participants will aid in developing study-related treatments. This may include informing the treatment schedule for the intervention, advising the outcome measures of most importance to them, and helping refine study-related forms. Through collaborating with people who have personally experienced the challenge of stroke recovery, we hope to develop more patient-centered and relevant interventions.

For the Trial proposed, Veterans with upper extremity hemiparesis due stroke in the brain (including brainstem) are the focus of this study. The subjects, males and females of all races and ethnic origins, are expected to be between 18 and 88 years old. There are no targeted populations for this study. The study will recruit Veterans with acute hemiparesis resulting from injury to the brain due to stroke (including brainstem) as inpatients at the Minneapolis VA Health Care System and who meet all the inclusion criteria and none of the exclusion criteria, regardless of race, sex, or ethnicity. Vulnerable populations will not be targeted. There will be no children participating in this study. Inclusion and exclusion criteria are indicated in the table below.

Table 3. Inclusion and Exclusion Criteria

Inclusion	Exclusion
Veterans between 18 and 88 years of age	Complete loss of arm function
Inpatient at the Minneapolis VAHCS.	No contact address or telephone
Willing and able to give Informed Consent or meets criteria for surrogate consent	Active substance use disorder or Major uncontrolled psychiatric disorder
Upper extremity hemiparesis resulting from stroke in the brain (including brainstem) or tumor resection at the discretion of the therapist.	
Lives within vicinity of the Minneapolis VA	
Has either a computer monitor or TV at home the participant will allow the gaming device to be connected to.	

Patients meeting study criteria who consent to participate will be consented and enrolled in the study. Additional recruitment will be pursued if a participant chooses to leave the study prior to completion. Subjects will participate in the study while as inpatients at the Minneapolis VA and for up to 3 months post-discharge. Motor function for all subjects will be assessed prior to treatment (baseline), before discharge from the hospital, and at a 3-month follow-up appointment. A clinician Assessor-OT (A-OT) will conduct these assessments. Subjects will be compensated for their participation in the study in three $50 disbursements: following the initial baseline assessment, following the assessments conducted at discharge, and following the 3-month follow-up appointment.

For all study participants, Occupational Therapy staff will conduct evaluations as usual that may include: Manual Muscle Testing (MMT), Range of Motion (ROM) measurements, and cognitive skills testing. They may also include many activities that are conducted at bedside, such as dressing, grooming, and showering. The subjects will be encouraged to participate in at least 3.5 hours of independent game play per week. Subjects will complete 1.5 hours/week dedicated to the â€œTransfer Packageâ€ during regular OT sessions. The other 3.5 hours of OT therapy will still be conducted and will bring total therapy time to 5 hours/week.

Once discharged, all participants will be encouraged to keep a log of adherence to the prescribed home exercise program. The specifics of each home exercise program cannot be known at this time, given the individual progress study participants may display. Participants will be given the option of bringing the gaming system home for continued gameplay. Prior to discharge research staff will determine if a home visit is necessary for setting up the gaming system. Participants who are able to set up the system themselves or with the assistance of a caregiver will not necessitate a home visit, though a phone call may be used if minimal assistance is needed. If needed, research staff will make a home visit to the homes of subjects participating in the active intervention portion of the study to ensure proper set up the gaming system and to reinforce use of the system. The study coordinator will train all study participants in the use of training and smartwatch compliance logs prior to discharge from the medical center. If an in-person visit isnâ€™t possible due to COVID-19 restrictions or other unforeseen issues the study team will discuss feasibility of having the participant set up the system with assistance from study personnel via phone or teleconferencing. If study clinicians determine that performing this setup would be too difficult for participant to do without in-person assistance, the subjectâ€™s participation will end at time of discharge.

During the at home portion of the study, training logs and smartwatch compliance logs will be employed. The study coordinator will call participants every two weeks post discharge, and as needed, until study participation has been completed. These phone interactions are intended to facilitate the proper use of the smartwatch device and to monitor self-reported compliance. The smartwatches will collect activity data on all subjects. There is a built-in data collection mode that allows for information on general activity level to be collected. Because the watchesâ€™ memory capacities are filled after one monthâ€™s use, replacement watches will be sent approximately 3 weeks into the month of use to ensure that a replacement watch can be sent and received in a timely fashion. This will permit the next monthâ€™s data to be recorded. The study coordinator will facilitate the exchange of the equipment in a timely manner so that there is no disruption in the data collection. During the telephone calls, subjects will be asked questions such as, â€œHave you taken either smartwatch off for any reason in the past two weeks?â€, â€œHave you received your replacement watch in the mail?â€, â€œDo you have any concerns regarding the proper functioning of your smartwatch?â€.

Table 4. Timetable of Participant Activity

Contact	Week	Approximate duration (minutes)	Remuneration	Administered by
Referral from Clinician	-1 or 0	5		PI, SC
Initial Study Contact	-1 or 0	15		SC
Consenting Process Initiated	0	60		SC

Screening for Inclusion and Exclusion Criteria	0	15		OT or COTA, and SC
Baseline Assessment	0	60	X	A-OT
Initial Gaming Set-Up	1	30		OT or COTA, PI, SC
Standard of Care- **Inpatient**	1-3, 5x/week	30-60		OT or COTA
Transfer Package- Inpatient	1-3, 3x/week	30		OT
Gaming- Inpatient	1-3	10min 3x/day		OT or COTA
Conclusion of Usual Care- Assessment	3	60	X	A-OT
Post-Discharge Home Visit to set up gaming system	3	60		PI
Outpatient	Home Exercise Plan â€“ varies dependent on individual patient progress			
Gaming- Outpatient	3x/week	30		Subject
Follow-up Visit- Assessment	12	60	X	A-OT

OT- Occupational Therapist, A-OT- Assessor Occupational Therapist, COTA-Certified Occupational Therapy Assistant, SC- Study Coordinator,
PI- Principal Investigator

Potential subjects will be referred to the PI or Study Coordinator (SC) by clinician members of the Study Team. The PI or the SC will meet with the potential subject to discuss the details of the study and to answer any questions that the Veteran has about study participation. If the potential participant meets all the inclusion criteria and none of the exclusion criteria an appointment for the initial visit will be made. At this visit, the informed consent process will begin, and consents will be obtained, including the Authorization for Use and Release of Individually Identifiable Health Information Collected for VHA Research will be obtained, and the Consent for Production and Use of Verbal or Written Statements, Photographs, Digital Images, and/or Video or Audio recordings by VA. The subject will be given ample time to ask questions, confer with family regarding participation in the research study, and to have questions answered. If the patient lacks decision-making capacity, the surrogate consent process will be employed with the patient and their Legally Authorized Representative/Personal Representative (described below in section 2).

Should the study coordinator not be able to meet with the participant in-person, consent may be done over the phone or via a VA approved teleconferencing system, with a study clinician available in-person to assist as needed. When consenting subjects via phone or teleconferencing system, all participants will have a physical copy of the consent/assent and HIPAA forms to be signed in wet ink. Copies of the singed consent/assent and HIPAA forms will be given to the participant, study records, and the IRB. A study clinician may be there in person to assist with the forms and technology set up. A wet in signature will be obtained before any study activities begin.

If the study coordinator or any research personnel are unable to interact with the participant in-person (e.g., due to the COVID-19 related administrative hold on research), in-person study visits may still take place with a study clinician only if the clinician is already seeing the inpatient clinically, as part of their regularly scheduled OT. All hospital mandated safety and PPE requirements will be followed.

Sources of Materials. Sources of material for this study will be subject interviews (e.g.-demographics and assessment instruments), existing computerized patient record system (CPRS) records, and data obtained from the research intervention itself (activity data collected by biofeedback devices). OT clinicians will write several types of notes in the medical record that will serve as a source of information for tracking usual care interventions and changes in health status for inpatient study participants. our OT evaluations (as usual) include MMT, ROM, Box and Block, Nine Hole Peg Test, and Action Research Arm Test (ARAT) The study coordinator will extract information from the OT Consult Note, OT Evaluation Note, OT Progress Note, the OT Discharge Note, and along with other information present in the medical record to capture differences in the rehabilitation treatments. For those in the outpatient setting, each subject will be given a study diary will contain a checklist to be used daily and will collect information including what interventions were used each day, and the intensity, duration and frequency for those interventions.

Potential outcome measures include the ARAT, Wolf Motor Function Test (WMFT), the Fugl-Meyer Assessment, the Neuro-QoL, and the QUEST 2.0.

During the study, arm use during daily activities (a potential moderator of improvement) will be tracked via a smart watch application. Participants will be encouraged to wear a smartwatch on each wrist during the inpatient stay and post-discharge until the 3-month follow-up visit.

Potential Risks. There is no therapeutic risk involved in the study. The risks associated with this study are research risks. The risks associated with the CI therapy in this research study are no greater than would be encountered in standard care. Research risks to the subjects include possible physical side effects from gaming. These physical risks include strained muscles and joints. The chance of these effects occurring is no greater than for gaming performed in daily life. Subjects will be encouraged to play for at least 10 minutes three times daily, thereby minimizing the risk of strain. There is a slight chance of these risks occurring.

Personal questions, including demographic information will be asked on an initial questionnaire. Measures of impairment and quality of life will also be administered. Subjects will answer the questions in a quiet room; privacy will be considered and protected. There is a slight possibility of psychological risk if answering the questions causes a subject to become uncomfortable. These questions pose minimal social and legal risk.

Because CPRS will be accessed for recruitment, payment purposes, and for the writing of the Research Participant Progress notes, there is a minimal risk that private personal information can be accessed for fraudulent purposes.

Subjects may experience economic harm by participating in the study, such as additional transportation costs to travel to the facility and possible lost wages due to time missed from work once the participant is

an outpatient. The subject remuneration will be compensation for time and inconvenience. To minimize this potential harm, subjects will receive $50.00 for each study visit.

2. Adequacy of Protection from Risk
Recruitment and Informed Consent. The potential study participant will meet with the Study Coordinator in the patientâ€™s hospital room or other more private location if needed, or via phone/teleconferencing system. They will discuss the consent and HIPAA forms. Keeping in mind the subjectâ€™s privacy, the coordinator will speak discreetly with the Veteran. A description of the study, the purpose of the study, the benefits and risks of participation, research subjectâ€™s rights, disclosure of protected health information and the subjectâ€™s right to confidentiality are among the items covered in the consenting process. The Study Coordinator will be up to date with all required trainings including CITI Training and VA Information Security.
A potential study participant will have the opportunity to ask questions about the study and have questions answered. The Study Coordinator will ask several open-ended questions to assess the potential subjectâ€™s level of understanding. If the veteran agrees to the content of the consents and HIPAA forms, he or she will voluntarily sign them. Study subjects will receive a copy of the consent form and HIPPA. Consent and HIPAA forms will be copied and sent to Research Compliance Officers for auditing. The original forms will be scanned into a secure folder behind the VA firewall. These forms will be stored in a locked cabinet in the research laboratory.

Surrogate consent will be used if it has been documented by a qualified practitioner in the patientâ€™s medical record in a signed and dated progress note that the patient lacks capacity to make important decisions or if the individual has been ruled incompetent by a court of law. If the potential subject does not have this documentation, but there is a question about their decision-making capacity, the researcher will consult with a qualified practitioner about the individualâ€™s decision-making capacity before proceeding with the informed consent process. For potential participants deemed non competent, the patient's legally authorized representative (LAR) will be approached about the study regarding possible participation by providing surrogate consent. The LAR may be the Durable Power of Attorney for Health Care (DPAHC) but also next of kin in the following order: spouse, adult child, parent, adult sibling, grandparent, or adult grandchild. The LAR will be asked to make the decision based on what the subject would do if competent or if unknown/unable to ascertain, what they feel is in the participant's best interest. The proposed research will be explained to the potential subject in language at a level they are able to understand and will be asked to sign an assent form stating that they voluntarily assent to be in the study. Under no circumstances will a subject be forced or coerced to participate in the study, even if the surrogate has provided consent. The HIPAA form will be discussed and signed with the patientâ€™s Personal Representative, who must meet one of the following requirements; 1) Power of Attorney (POA) for decisions related to health care, 2) legal guardian designation by a court, or 3) Authority to Act on behalf of the individual under other federal, state, local, or tribal law. If the participant regains decision-making capacity, the investigator or study coordinator will repeat the informed consent process with the participant and obtain the participantâ€™s permission to continue with the study.

Because informed consent is a process, rather than a onetime event, the study subject will be encouraged to ask questions that may arise throughout the course of the study.
Following the consenting process, the subject will have a screening exam by a study clinician to assess the Veteran for inclusion and exclusion criteria. A Research Participant Note will be written in the subjectâ€™s medical record and a flag created to notify other CPRS users that the subject is enrolled in an interventional study at the Minneapolis VA Health Care System. This flag will warn of participation in an interventional study and act to prevent possible dual enrollment, thereby protecting the subject from potential risks involved in participating in two studies concurrently.

Protection Against Risk. Participants in the study will be closely monitored by the clinical study staff. Study subjects in the standard care group and those in the CI Therapy group will report any unexpected changes or concerns to the study team. In compliance with VA policy, any unexpected, serious, related/probably related adverse event will be reported within 5 business days to the IRB. Serious events that are not both unanticipated and related will be reported at continuing review. When consenting to participate in the study, the subject will sign also sign a HIPAA form giving the study staff permission to access his or her medical record. All study staff realize the importance of keeping private personal information secure and are trained annually by the VA to minimize this risk.

Data Security and Sharing. All VA sensitive research data for this protocol recorded on paper records, especially participant PHI, will be stored in a locked file cabinet, in a locked lab, inside a security card controlled research wing of the hospital. It will be available and used only by approved study personnel. The Investigators and Staff will ensure the proposed research follows relevant privacy, confidentiality, and information security requirements. The Research Privacy Officer (RPO) and Information Security Officer (ISO) review the proposed study protocol and any other relevant materials when they are submitted in the IRB application. During the study, the RPO and ISO will conduct assessments to ensure that all applicable local, VA and other Federal requirements for privacy and confidentiality, and for information security have been met.

3. Potential benefits of research to subjects and others.
The intervention has provided promising results in other treatment environments though these benefits cannot be assured. The knowledge gained through the conduct of this pilot study may benefit others in the future.

4. Importance of knowledge to be gained.
The proposed work will establish the initial efficacy and feasibility of supplementing inpatient rehabilitation with video-game based treatment in an inpatient setting. The proposed work is the initial step towards a program of research that will examine the feasibility of this approach, incorporate a longer follow-up period, establish patient characteristics that predispose individuals to a favorable response, and include cost-effectiveness measurement. The result of this research program would be evidence that could transform rehabilitation policy, lower costs, and enhance the way that inpatient rehabilitation care is delivered.

Data and Safety Monitoring Plan. To minimize risk, all VA sensitive research data for this protocol, including subject data and PHI, will be stored on a secure VA server behind the necessary VA firewalls. In addition, data recorded digitally over the course of the study will be saved in a secure folder behind the VA firewall. Only approved study staff and administrators will have access to this secure data folder. This is done in accordance with the Minneapolis Research Service Data Security Plan. The PI will ensure that all data storage locations will be kept current in the Minneapolis VAHCS Data Inventory database.

To preserve privacy only de-identified, anonymized dataset will be created and shared. The PI will provide oversight for the security of the data and conduct of the study.

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