Protocol Summary: Telerehabilitation early after stroke
February 17, 2022

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Brief summary

Stroke is a major cause of disability. Loss of movement is a major part of this. Studies show that high doses of rehabilitation therapy can reduce disability, but many patients do not receive this, e.g., due to obstacles such as difficulty accessing care. We have previously found that telerehabilitation is an effective way to deliver care and improve outcomes. These prior studies were performed after hospital discharge, when patients were already back at home. The current study aims to extend this work by introducing telerehabilitation to the bedside of patients admitted to an inpatient rehabilitation facility (California Rehabilitation Institute and MossRehab). In this study, we will measure issues and effects of telerehabilitation that is started during the rehab admission and is continued after discharge in the patient's home.

The study will be conducted at two sites: California Rehabilitation Institute (Los Angeles, CA) and Moss Rehabilitation Research Institute hereafter "MRRI" (at MossRehab, Elkins Park, PA). UCLA IRB will be conducting all reviews for MRRI.

Data Security Plan

Data security focuses on four aspects of the data:

1. Hard copy case report forms: These are the paper forms used during patient evaluations. These are stored in locked rooms in a secure area of Cal Rehab and MRRI that cannot be accessed by the public.
2. The telerehab computer: This is the Windows computer that each patient uses to engage in telerehab. The same computer device is used while the patient is admitted to Cal Rehab (or Moss Rehab) and once at home. This computer used by the subject will hold some identifiable data (specifically, at UCLA, photos of the patient playing therapeutic games; and at both UCLA and MRRI, scores on computerized assessments). These computers are secure by virtue of being housed physically in the patient's own hospital room (Cal Rehab) and/or the therapy area (MRRI), or in the patient's own home, after discharge from the inpatient rehabilitation facility. These computers cannot be accessed without specific passwords. All traffic in/out of these computers is over HTTPS and thus is encrypted.
3. The server: A copy of all patient-related data (usage statistics, performance data such as game scores, plus the above-mentioned photos and scores on computerized assessments) is copied from the patient's telerehab computer to a server, in real time. This is how the therapist who has logged into the system is able to view his/her patient's usage/performance statistics, and this is how the study team is able to review such data when it comes time to analyze/publish study results. All such data collected at UCLA for the proposed study will use a secure server specifically managed by the DGIT group at UCLA. Data collected at MRRI will be hosted on TRCare server and will be shared via email to UCLA or uploaded to a secure shared box folder by the team at MRRI.
4. Extracted data: Patient data are extracted from the case report forms (e.g., scores on scales that are tested) and from the server (e.g., usage statistics or computerized assessments) and then saved into data files (e.g., in xls format). These data files are what the team uses for statistical analyses. These data files are password protected and only copied onto password-protected computers that are always kept in a locked room. Furthermore, there is a separate file that contains key PHI (e.g., name, contact data) and is linked to the data file through a study ID. In this way, the data file has little or no PHI.

Regarding use of data that includes personal identifiers:

(a) Treatment of personal identifier information maintains all of the security procedures and standards described in the Data Security Plan. Thus, when such information appears on a hard copy form, that form remains in a locked room in a secure non-public area of the hospital. When such information appears in electronic form, it is in a password protected file on an encrypted computer in a locked room.
(b) Confidentiality is assured by maintaining security, as in (a), and by limiting access to these secure files to persons approved on this IRB application.
(c) Access to identifier information will be limited to personnel approved by the IRB, i.e., the research team supervised by Dr. Cramer at Cal Rehab, and the team supervised by Dr. Edwards at MRRI.

Specific Aims

There are 3 Specific Aims to be addressed by this study:

1. Assess the feasibility of initiating telerehab during admission to an inpatient rehabilitation facility
2. Evaluate the patient experience and (when available and consented) the caregiver experience
3. Measure patient outcomes at the end of a 6-week course of telerehab, particularly with respect to motor outcome, functional outcome, and mood outcome.

Background and Significance

Patients need higher doses of high-quality rehabilitation therapy: Stroke remains a leading cause of human disability. Motor deficits are a substantial contributor to this, particularly in the arm: few patients fully recover from arm weakness after a stroke, with the remainder demonstrating persistent arm impairments that are directly linked to larger activity limitations and participation restrictions, lower quality of life, and decreased well-being[1-3].

Increasing evidence suggests that intensive activity-dependent therapy can improve outcomes. Rehabilitation therapy dose after stroke can be examined as repetitions per session. In mice with ischemic brain injury, 200 was superior to 100 forelimb reaches/day for improving increasing the rate of functional improvement[4]. Jeffers et al found that in rats, in order to realize functional benefits in the most severe cases, the required intensity of rehabilitation was “upwards of 600-700 repetitions per day”[5]. Primate studies of stroke recovery target 600[6]-924[7] movements/day. Birkenmeier et al[8] noted that "These paradigms collectively suggest that hundreds of repetitions of task-specific practice may be required to optimize function post stroke."

However, most patients do not receive such therapy for reasons that include difficulty traveling to a provider, shortage of regional rehabilitation care, and poor compliance with assignments. Furthermore, even when patients can access stroke rehabilitation, the amount of therapy provided in standard of care is limited [9-13], averaging just 32 arm movements/session[9].

The quality of rehabilitation therapy is also important and can increase the extent to which clinical neuroplasticity is harnessed[14]. Effects are increased when therapy is challenging, motivating, and engaging[15-18].

The promise of a telehealth approach for increasing rehabilitation therapy: Telehealth approaches have the potential to address these issues by increasing access and by boosting motivation. Telerehabilitation (TR) is the delivery of rehabilitation services via communication technologies[19]. TR is delivered by a licensed therapist via a computer and over the internet, often asynchronously, but follows the same principles of traditional, person-to-person, individualized rehabilitation care. Such telehealth therapy provides a powerful supplemental option to brick-and-mortar delivery of rehabilitation services[20-23], reducing the need for impaired patients to travel and increasing access to care by clinicians familiar with stroke rehabilitation, especially in regions with a shortage of providers. These points are underscored in times of quarantine. Furthermore, even if TR is found to be merely equivalent to usual care, TR could be of value to many patients as an alternate form of therapy delivery, a need also highlighted by the recent pandemic.

Because TR incorporates a computer, therapy can be provided via games, which promotes patient participation in health care[24-28]. Games motivate patients to engage in enjoyable play behavior that involves therapeutically relevant movements[29-31], important because patient compliance with stroke rehabilitation is often limited[32-34]. TR can also reduce the burden on caregivers and increase compliance; costs might also be lower[35] but this issue will not be examined in the currently proposed clinical trial.

Mounting evidence that TR helps with motor deficits after stroke: Increasing data support the utility of motor TR. A recent meta-analysis reported that all 18 studies of post-stroke motor TR improved motor disabilities[23]. Another noted that effects of TR did not differ from those seen with in-person rehabilitation or usual care, although findings from this review must be viewed cautiously given that the authors defined telerehabilitation quite broadly, e.g., including interventions that relied on phone calls, DVDs, email, online chat rooms, etc[36]. Other reviews indicate that higher TR usage results in greater benefit[37], although to date many studies have been small and uncontrolled[23, 37-40]. In one recent review of neurotechnological interventions for upper-limb motor rehabilitation, Coscia et al[41] stated

“We also promote the necessary conceptual change from ‘one-suits-all’ treatments within inpatient clinical rehabilitation set-ups towards personalized home-based treatment strategies by adopting novel technologies….”

In this regard, it is important to note that the current proposal employs a telehealth intervention that is structured and therapist-supervised, and designed for use in the home[42]. My lab has published three TR studies to date (reprints of which are attached to this application).

The TR program to be employed in the currently proposed study directly emulates the successful approach used in our prior national trial[43]. This is an approach that worked--it produced large gains in patient function across enrollees at 11 US sites--I am not changing an effective therapy. Instead, here I aim to apply this very same therapy to a population of patients who are at an earlier time point post-stroke.

The rationale for using this 6-week (42-hour) program of therapist-supervised, home-based TR: This is an effective dose of an effective therapy and so treatment dose and content will not be modified when addressing current hypotheses. **The prior national trial[43] found that 6 weeks of TR was safe and associated with substantial gains in UE-FM, Box & Blocks, and mRS scores, among all patients as well as among patients enrolled >90 days post-stroke**. Thus, current goals do not aim to change the intervention but instead to examine short- and long-term TR effects in relation to usual care.

Prior studies of TR from the Cramer lab:

(1) A pilot study of TR: In our pilot study[44], 12 patients with chronic stroke underwent 4 weeks of home-based, therapist-supervised TR targeting arm motor deficits. We found that

1. Patients were highly compliant (97.9% of assigned days) and rated the system favorably.
2. Therapists in the clinic were readily able to remotely review patient performances and revise therapy.
3. Videoconferences successfully supported regular communication between the patient and treatment team;
4. Arm motor status improved significantly overall and exceeded the minimal clinically important difference in half of the patients.
5. Daily stroke education significantly increased stroke prevention knowledge.
6. Screening for depression using telehealth methods was accurate.
7. All of these findings were unrelated to patients' computer skills, as a measure of computer literacy was not related to treatment gains or system usage level.
8. With 60 min/day of TR, patients averaged 879 arm repetitions per day.

As above, preclinical studies indicate that hundreds of limb movements/day are needed to achieve optimal post-stroke motor cortex plasticity[45], and substantial evidence indicates that higher doses of activity-based motor therapy after stroke are associated with improved outcomes [46-50], yet **patients receive only 32 repetitions per session in routine clinical care**[9]. TR may be able to bridge this gap and provide high doses of intensive therapy.

(2) A separate study of 12 patients with chronic stroke documented our ability to improve visuospatial functions using home-based TR[51].

(3) A multisite, randomized, assessor-blinded trial of TR: Subsequently, my lab led an 11-site national trial[43] run in the NIH StrokeNet clinical trials network (of which I am co-PI). The primary aim was to determine whether treatment targeting arm movement delivered via a home-based TR system has comparable efficacy with dose-matched, intensity-matched therapy delivered in a traditional in-clinic setting. A randomized, assessor-blinded, non-inferiority design was employed. Entry criteria included stroke with onset 4-36 weeks prior and arm motor deficits (defined as Fugl-Meyer score of 22-56 of 66). Patients were randomized to TR therapy in the home or therapy at an outpatient clinic. All enrollees received 36 sessions (70 minutes each) of arm motor therapy plus stroke education. Therapy intensity, duration, and frequency were matched across groups.

The main results of this multisite, randomized, assessor-blinded trial are as follows: The 124 enrollees had baseline FM score of 43±8 (mean±SD) points, and were enrolled 18.7±8.9 weeks post-stroke (anywhere from 4-36 weeks post-stroke was allowed). Compliance was 98.3% in the TR group and 93.4% in the in-clinic group. Change in Fugl-Meyer score from baseline to 1-month post-therapy (the primary endpoint) was 8.4±7.0 points for the in-clinic group vs. 7.9±6.7 points in the TR group. The covariate-adjusted Fugl-Meyer score change was 0.06 (95% CI -2.14, 2.26) points higher in the TR group ($p=0.959$); the non-inferiority margin fell outside this 95% CI, indicating that TR is not inferior to in-clinic therapy. Motor gains remained significant when patients enrolled early (<90 days) or late (>90 days) post-stroke were examined separately. Motor gains were also significant when examining change in the Box & Blocks score, a measure of arm function (activities limitations). Stroke Knowledge scores increased significantly ($p<0.001$).

The number of arm movement repetitions over 36 TR treatment sessions was calculated in a convenience sample. **With 70 min/day of TR, patients averaged 1,031 arm repetitions per day**.

In sum, a 6-week course of daily home-based TR supervised by a licensed OT or PT was safe, rated favorably by subjects, associated with excellent treatment compliance, and produced substantial gains in arm function that were not inferior to a dose-matched intervention delivered in the clinic.

Summary: Stroke is a leading cause of disability. High dose rehabilitation therapy can reduce this disability but in current practice is often fragmented and abbreviated. As a result, an overwhelming majority of patients do not receive the fullest dose of rehabilitation therapy to improve outcomes. There are a number of reasons for this, including regional availability of therapists, the logistics of arranging travel back and forth to a therapist's office, the challenges some patients face when transported, and dosing limitations placed by some insurance companies.

The current study represents an initial foray into providing care at earlier time points after stroke, a time when the brain is galvanized for plasticity[14].

Telehealth-based therapy provides a powerful supplemental option to brick-and-mortar delivery of rehabilitation services[23], reducing the need for impaired patients to travel and increasing access to care especially in regions with a shortage of providers. Because TR incorporates a computer, therapy can be provided via games, which promote patient participation in health care[24-28], and motivate patients to engage in enjoyable play behavior that involves therapeutically relevant movements[29-31], important because patient compliance with stroke rehabilitation can be limited[32-34]. A computer enables remote patient assessment, including of motor deficits, pain, and depression[43, 44, 51, 52]. A computer also enables live videoconferences between a patient and a licensed OT or PT, a feature rated very highly in our qualitative study of home-based TR[53]. The therapist can also interact with the patient asynchronously, monitoring usage and performance statistics and modifying treatment content any time of day. TR can also reduce the burden on caregivers and increase compliance.

Research Design and Methods

Study Procedures

Patients who are potentially eligible will be identified from review of daily admissions. Those who have a diagnosis of stroke will be pre-screened through chart review. Those who are deemed potentially eligible will be approached. The study will be explained and all questions answered. Patients will then be asked to sign informed consent, as well as the UCLA HIPAA Authorization form (which is used to acquire medical records from outside Cal Rehab). If the patient (a) has a caregiver and (b) that caregiver is interested, he/she will also be offered study participation.

For caregivers who sign consent, he/she will be asked a series of questions about expectations and experiences with TR. This will occur twice, once at the start of the study and once at the end of the study.

For patients who sign consent, Visit 1 testing will ensue, the initial purpose of which is to fully confirm study eligibility. Patients who meet all entry criteria, and no exclusionary criteria, will then complete Visit 1 testing. Visit 1 testing may be completed over more than one day, as needed.

[UCLA ONLY: For genetic testing, DNA and genotyping data will be collected from patients under the protocol described in IRB#10-01577 using an iPad consent process. IRB#10-01577 includes a biorepository that allows sharing of data and samples. Data and DNA samples will be shared back to the currently proposed study. Blood for genotyping will be taken from pre-existing specimens already in the laboratory; on occasion, an additional tube of blood may need to be drawn].

Once testing is completed, the patient will be introduced to the TR system, which may occur in the patient room, a designated study room, or in the inpatient therapy area. During the rehab admission, each system may have multiple users. However, each patient will be assigned an itinerary specific to his/her abilities and needs. Once one patient has completed all study procedures, the TR system is returned to the lab.

Each patient's TR therapy program is designed, administered, and supervised by a licensed occupational therapist (OT) or physical therapist (PT). This begins with review of the medical record and Visit 1 data, then a live exam. The therapist at the enrolling site then uses the therapist-facing study software to design an initial 70-minute treatment session. The therapist electronically pushes this treatment session onto the patient's TR computer, silently, and this can be done at any time. The patient is prompted by the computer (at a time of day suggested by the patient) to begin the session and then engages the TR system until the day's 70-minute session is completed, taking as many breaks needed, of any duration.

Using the therapist-facing study software, the therapist is able to monitor usage and game performance statistics and create successive day's therapy programs. The therapist has a 60-minute videoconference with

the patient three times/week, using the HIPAA-compliant VSee software at UCLA and Zoom for healthcare at MRRI. (The videoconference may be shorter in duration if the patient ends the session early and will exceed this value only as needed per clinical judgment.) In this way, the therapist maintains an ongoing relationship with the patient (a feature rated very highly in our qualitative study[53], which is attached to this application) and is also able to see the patient performing rehab exercises and games and provide appropriate feedback.

Once the patient is ready to go home, his/her TR system is unplugged and prepared for home delivery. Once the patient has reached home, our team delivers the TR system to the patient's home, sets it up, and connects it to the internet using either the patient's home WiFi system or a Verizon MiFi modem provided by the study if WiFi is not available. Home delivery and setup in this manner is precisely the approach used in in our prior national trial[43]. If the patient is discharged to a different destination, we will make every effort to continue TR at that site.

The patient then completes 36 treatment sessions over 6 weeks, consisting of 3 sessions/week that are supervised TR sessions alternating with 3 sessions/week of unsupervised TR sessions whereby the patient follows the instructions on the screen to engage in TR. Because patients sometimes miss a session (e.g., due to a conflict), we allow up to 8 weeks for patients to complete their 36 TR sessions. The supervised home telerehab intervention sessions may be exclusively provided by the enrolling site, exclusively provided by the collaborating site, or a shared supervision as jointly decided by the study investigators based on available staffing. The initial treatment schedule will be designed by a therapist at the enrolling site and may be modified as and when needed by a therapist from the enrolling or collaborating site. In cases of joint supervision, the familiarization occurs by the local study team member will include at least one session of virtual introduction to the collaborating site staff member assigned to some/all of the remote supervision days. Text message reminders and phone calls from the staff member assigned to remote supervision days may be used during the intervention period. All telecommunications with participants will use HIPPA-compatible platforms such as Zoom for Healthcare (MRRI) or Vsee (Cal Rehab) and 8 x 8 or similar Voice Over IP platform (MRRI) or lab mobile device provided to the study therapists (Cal Rehab). One local contact person will be assigned for each participant at the enrolling site in order to address any local issues or questions that may require medical records review, adverse event reporting, home visit for device troubleshooting etc. Serious adverse events that may arise will involve Principal Investigators from both sites for review and reporting for participants who have shared supervision sessions.

After the 36 sessions are completed, or after 6-8 weeks from the first session, the team will return to the patient's house (Cal Rehab only) or invite the patient to the institute (Cal Rehab and MRRI) to complete the Visit 2 assessments. The TR systems will then be removed from the patient's home and brought back to the respective laboratories at Cal Rehab and MRRI, where they will be carefully cleaned, and then made available to the next study enrollee. If at the time of Visit 2, a patient presents with symptoms suggestive of COVID-19, the patient may be asked to obtain a COVID test, at the discretion of the therapist. The COVID test may be provided by the study team or obtained independently by the patient (e.g., from a healthcare provider or a testing site). Alternatively, the patient may choose to reschedule Visit 2 at a time that is 10 days after the first sign of their COVID-related symptoms. As such, Visit 2 assessments in a patient with symptoms suggestive of COVID-19 would be completed either after confirmation of a negative COVID test or after a 10-day period.

The data collected using the same protocol at Cal Rehab and MRRI will be combined in a single joint report at study's end.

Schedule of Study Events

Test	**Visit 1**	**TR-based therapy and assessments**	**Visit 2**
	During IRF admission	Weekly, at IRF, and at home	6-8 wks after Visit 1
Obtain Informed Consent	X		
Confirm Eligibility criteria	X		
Medical History	X[a]	X	X
Chart review, including acute admission and imaging; IRF admission	X		X
Behavioral Contract	X		
Interview regarding preferences, likes/dislikes	X[a]		X[a]

Arm Motor Fugl-Meyer Scale	X		X
Box & Blocks Test	X		X
Montreal Cognitive Assessment	X		X
3 Rehab Practice Tasks			
Geriatric Depression Scale	X		X
Visual Acuity Screen	X		
Caregiver Strain Index	X*		X*
NIH Stroke Scale	X		
modified Rankin Scale	X		X
SAFE Score	X		X
Nottingham Sensory Assessment	X		
Handedness Inventory	X		
Line Cancellation Test	X		
Trail Making Test (TMT): Part A & B	X		X
Language Screening Test	X		
Grip and Pinch Strength	X		X
Nine Hole Peg Test	X		X
14-item Motor Activity Log	X		X
Review of TR System	X		
modified Ashworth Scale	X		X
Arm or Shoulder Pain		X[c]	
Fatigue		X[c]	
Daily Motor Testing		X[c]	
Finger Tap Assessment		X[c]	
Stroke Knowledge Exam	X		X
Record amount of rehabilitation therapy received outside of study procedures	X	X	X
Telerehabilitation Therapy (36 sessions)		X[c]	
Stroke Impact Scale-ADL Subsection	X		X
Stroke Impact Scale-Hand Subsection	X		X
EuroQoL-5D	X		X
Genetic testing	X		
Proprioception testing	X		
3D Movement Kinematics Test	X		
Chaos Scale		X[b]	X
General Anxiety Disorder – 7		X[b]	
Patient Health Questionnaire (PHQ-9)		X[b]	
Brief Resilience Scale		X[b]	
Mental Adjustment to Stroke Scale – Fighting Spirit Subsection		X[b]	
MOS Social Support Survey		X[b]	
PROMIS Physical Function Scale			X
PROMIS Social Roles/Activities Scale			X
Adverse Events		X	X
Patient Satisfaction with Telerehabilitation Survey			X
COVID-19 screening/test (as needed)			X

[a]Indicates testing that will also be performed on a caregiver, if one is available and also signs consent.
[b]Indicates testing will be performed only once during 6-week period

[c]Will be completed at least 6 days a week
*will only be administered to caregivers who signed the caregiver informed consent

Further details of the TR intervention:

TR is delivered over 36 sessions, each of 70-minutes duration. Half of the sessions are supervised by a licensed OT or PT (the goal is to work with the same therapist for 6 weeks) and half are unsupervised. To account for possible extrinsic events (e.g., illness or vacation), patients are permitted up to 8 weeks to complete these 36 treatment sessions.

A therapist-facing web portal is used for treatment planning and patient monitoring: All treatment is generated and supervised by a licensed OT or PT. Therapists use a graphical interface to drag treatment components (individual exercises and games) into a 70-min planner for each treatment session; they then adjust the difficulty and duration of each treatment component. The initial treatment plan is generated using a study-supplied algorithm that suggests specific games and exercises based on scores on the 33 UE-FM exam components or based on the therapist's review of baseline assessments.

The same therapist-facing web portal allows therapists to review usage and performance statistics at any time, from any secure location. In this way, therapists can monitor patient compliance and performance, and can modify treatment content accordingly, at any time. The study imposes a formal requirement for a revised treatment plan after 2 and after 4 weeks.

Videoconferences: Supervised sessions begin with a patient-therapist videoconference, during which therapists supervise therapy, answer questions, review treatment plans, and perform selected study assessments. Therapists are also encouraged to discuss use of the UE in home.

During the 6 weeks of TR therapy, patients are permitted to receive outside therapy as part of usual care, the amount of which is recorded, as in the prior national trial[43].

All subjects sign a behavioral contract[54] that includes a personal treatment goal.

The treatment approach was initially designed based on an upper-extremity task-specific training manual[55] and Accelerated Skill Acquisition Program[56]. Provision of feedback to subjects is a core feature, on supervised days, based on therapist's videoconference observations plus therapist's review of electronic data (prior days' usage, scores, photographs during gameplay).

Each daily 70-minute treatment session is created by a licensed OT or PT and includes:

(1) At least 15 min/day of arm exercises. A total of 114 UE exercises are available, each consisting of a video showing the assigned movement. Therapists can also choose to demonstrate an exercise during videoconferences on supervised days. In addition, therapists have the option to incorporate standard exercise equipment (e.g., Theraband or putty) that is also provided to patients at the time the TR system is delivered to the home and that can be incorporated into assigned exercises.

(2) At least 15 min/day of functional training through games. A total of 12 input devices (e.g., PlayStation Move controller, input buttons, or trackpad) are available for use to drive game play. A total of 25 functional games are available. Games stress various motor control features (e.g., varying movement speed, range of motion, target size, extent of visuomotor tracking, or level of cognitive demand), which are selected and adjusted by the therapist. For example, during the whack-a-mole game, higher difficulty level means a broader area where targets can appear and a shorter duration of time to hit the target. Therapists also select the input device that the patient will use to play each game. For example, the flappy-bird game can be played using the grip force cylinder, pinch force cube, trackpad, or other devices.

(3) Five minutes/day of stroke education. The education content targets five categories (Stroke Risk Factors, Stroke Prevention, Effects of Stroke, Diet, and Exercise) and corresponds to the Stroke Knowledge Exam. At the start of unsupervised sessions, subjects answer multiple-choice questions, delivered via a video Jeopardy[57, 58] game format, then receive feedback.

The remaining 35 minutes consist of additional exercises and games, per the judgment of the licensed OT or PT.

Hardware: The TR system hardware consists of an internet-enabled computer with table, chair, and multiple gaming input devices--but no keyboard, as no computer operations are required by subjects.

During the 30 minutes prior to each session, the computer alerts the subject that the start time is coming soon. The subject hits a tabletop button to begin, and to start subsequent games/exercises. The TR software supports HIPAA-compliant videoconferencing between the therapist in the clinic and the patient at home. Supervised sessions will allow therapists to answer questions, review treatment plans, and perform study assessments. Unsupervised sessions have the same treatment content as supervised sessions but without

any therapist contact. Patients will be photographed during game play, and video recordings will be made during exercises, for therapists to review.

Key design features underlying the observed efficacy of this TR program include:

1. Treatment is supervised by a licensed OT or PT who generates the initial treatment plan after a live exam in the clinic, and who can remotely modify the treatment plan at any time.
2. The therapist maintains an ongoing relationship with the patient during the 6 weeks via the 3x/week videoconferences (a feature rated highly in a qualitative TR study[53])
3. An algorithm that uses the 33 UE-FM impairment measurements to suggest an initial treatment plan helps standardize the treatment approach.
4. Treatment is associated with a very large number of arm movements: 1,031/day[43], much higher than the 32/session[9] found during standard of care.
5. Use of games increases motivation and participation[24-31].
6. Patients have some control over their therapy (e.g., can pause TR to use the bathroom).
7. Patients sign a behavioral contract[54] that includes a personal goal, a commitment to incorporating the paretic UE into daily life, and a plan to incorporate TR into a daily pattern including starting TR therapy at the same time each day when possible.
8. The TR system has good variety, with five intervention categories (therapy, assessment, stroke education, prevention, and videoconferencing), 114 exercises, and 25 games.
9. The TR system is easy to use (e.g., with simple, large-font instructions; and provides both verbal and non-verbal cueing).
10. There is no need for computer literacy[44] (in fact, no computer keyboard is used).

Eligibility criteria are based on the prior national trial[43]:

Inclusion Criteria for patients with stroke

1. Age 18 years or older
2. Stroke that has been radiologically verified
3. Arm motor FM score <56 (out of 66) at Visit 1
4. Box & Block Test score with affected arm is at least 3 blocks in 60 seconds at Visit 1
5. Informed consent and behavioral contract signed by the subject (i.e., no surrogate consent)
6. Admitted to California Rehabilitation Institute or MRRI for stroke rehabilitation (Patients who have been recently discharged from the acute stroke hospital who otherwise meet entry criteria are also eligible.)

Exclusion Criteria for patients with stroke

1. A major, active, coexistent neurological or psychiatric disease, e.g., alcoholism or dementia
2. A major medical disorder that substantially reduces the likelihood that a subject will be able to comply with all study procedures
3. Severe depression, defined as Geriatric Depression Scale Score >10 at Baseline Visit
4. Significant cognitive impairment, defined as Montreal Cognitive Assessment score < 22 (a lower score is permitted if due to aphasia and if the patient is specifically allowed by the study PI)
5. Deficits in communication that interfere with reasonable study participation
6. Lacking visual acuity, with or without corrective lens, of 20/40 or better in at least one eye
7. Life expectancy < 6 months
8. Pregnant
9. Receipt of Botox to arms, legs, or trunk in the preceding 6 months, or expectation that Botox will be administered to the arm, leg, or trunk within 3 months of study enrollment
10. Unable to successfully perform all 3 of the rehabilitation exercise test examples
11. Unable or unwilling to perform study procedures/therapy or attend study visits, or expectation of noncompliance with study procedures/therapy
12. Non-English speaking, such that subject does not speak sufficient English to comply with study procedures
13. Expectation that subject will not have a single domicile address during the 6 weeks of therapy that has either Verizon wireless reception or a home WiFi network and that has space for the TR system.
14. Patients diagnosed, by medical personnel, with COVID-19, may proceed with study-related activities per CDC isolation guidelines.

Inclusion Criteria for caregivers

1. Age 18 years or older
2. Informed consent signed by the subject
3. Is a caregiver for a person with stroke who is eligible for this study and has signed informed consent

Exclusion Criteria for caregivers

1. Deficits in communication that interfere with reasonable study participation
2. Unable or unwilling to perform study procedures/therapy or attend study visits, or expectation of noncompliance with study procedures/therapy
3. Non-English speaking, such that subject does not speak sufficient English to comply with study procedures

Statistics and Data Analysis

This is a feasibility study. The purpose is to understand feasibility of this established therapy in a population admitted to Cal Rehab and MossRehab, to understand the experience from the point of view of patient and caregiver, and to document changes in motor and other behavioral outcomes. Results will be tabulated. Statistical moments will be calculated. The findings will be important to designing future TR studies in this target patient population. The sample size was selected to ensure that a representative experience is obtained across the very heterogeneous population that is subacute stroke, and is intended to approximate half the study size of the recent national trial.

Risks

- The possible risks and/or discomforts of this study are expected to be minimal.
- Patients may experience some fatigue and muscle soreness after moving the stroke-affected arm during rehabilitation practice.
- Study participation also carries the potential risk of general fatigue.
- Data are collected about patients and many videoconferences will occur. Despite intensive security efforts, data could nonetheless be stolen by thieves.

References

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