PROTOCOL TITLE:

Cognitive Priming to Boost Stroke Telerehabilitation Outcomes

PRINCIPAL INVESTIGATOR:

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1.0 Objectives / Specific Aims

The objective of this study is to investigate whether adding cognitive rehabilitation to an existing occupational therapy (OT) stroke telerehabilitation program will improve stroke survivors' daily functioning.

Aim: Implement cognitive rehabilitation as a primer for behavioral activation participation-based stroke telerehabilitation to enhance treatment outcomes. Hypothesis: We expect that this program will improve cognition (both objective and subjective measures), participation, upper extremity (UE) use in real-world activities, and mood/quality of life, generating effect estimates that will inform subsequent larger trials.

2.0 Background

An estimated 70% of stroke survivors have persistent cognitive impairment after clinical recovery[1], commonly in the domains of attention and executive function (e.g., cognitive control, working memory, cognitive flexibility)[2]. These multifaceted cognitive deficits are consequential for stroke recovery, with increased severity of cognitive impairment being associated with lower mood and quality of life, limited participation in daily activities, and more protracted disability[3,4]. Furthermore, post-stroke cognitive impairment (particularly executive dysfunction) may pose a barrier to successful engagement in rehabilitation treatments[5]. Our team developed a behavioral activation participation-based program for stroke survivors that we have successfully deployed in both face-to-face and telerehabilitation settings, led by occupational therapists (OT) and speech language pathologists. We have found that this intervention improves stroke survivors' abilities to participate in real-world home and community activities and reduces depression symptoms. Importantly, we observed that stroke survivors with more pronounced cognitive deficits at enrollment exhibit lowest participation in meaningful real-world activities, highlighting the need for such interventions in this subgroup. To effectively engage in this cognitively demanding telerehabilitation program, which requires metacognitive skills such as self-reflection and problem solving, stroke survivors may benefit from cognitive rehabilitation. Specifically, we propose that addressing cognitive deficits at the outset of this telerehabilitation program (i.e., cognitive priming) will improve stroke survivors' ability to benefit from this intervention by facilitating their learning, planning, organization, and goal management skills. Therefore, the proposed study will employ a titrated design in which we will first deliver sessions of evidence-based cognitive rehabilitation to improve attention and executive function followed by direct application of these new cognitive skills to the existing OT-led telerehabilitation program. Ultimately, we expect that integrating cognitive rehabilitation as a primer will enhance the efficacy of the telerehabilitation program, leading to improved participation in real-world meaningful activities.

3.0 Intervention to be studied

Participants will engage in a 10-week study of a stroke telerehabilitation program that incorporates cognitive rehabilitation and occupational therapy (OT). They will complete pre- and post-treatment assessments on weeks 1 and 10 and engage in the 8-week telerehabilitation intervention on weeks 2-9. The intervention consists of 13 telerehabilitation sessions lasting approximately 45–60min each (first 5 weeks: 2 sessions/week; final 3 weeks: 1 session/week). The overall goal of

the program is to improve stroke survivors' participation in home- and community-based activities. This study modifies an existing OT-led telerehabilitation program by adding cognitive rehabilitation to the initial sessions (see Table).

Week	1	2	3	4	5	6	7	8	9	10
Session	PRE	1-2	3-4	5-6	7-8	9-10	11	12	13	POST
Content	Pre Assessment	Cog Rehab	Cog Rehab	Cog Rehab + OT	Cog Rehab + OT	Cog Rehab + OT	OT	OT	OT	Post Assessment.

Cognitive rehabilitation will be therapist-led, one-on-one sessions focused on teaching cognitive strategies and their application to a broad set of activities/settings. The cognitive strategies will be in the domains of attention and executive function. The goal is to facilitate cognitive skill learning and generalization, by applying the new cognitive strategies to the participant's performance of home-based and community-based activities (taught through the subsequent OT-led telerehabilitation portion of the intervention). Cognitive rehabilitation interventions have been shown to produce small to medium effect size improvements in function for stroke survivors[6].

OT upper extremity rehabilitation will have 2 components: task-practice and metacognitive strategy training (both described in more detail in Section 10.0). The task-practice aspect of the intervention is considered current 'best practice' in stroke rehabilitation clinics. A task-practice intervention involves a patient repetitively practicing stroke-impaired movement skills within the context of a functional task to promote recovery of the impaired skills. In this study, participants will choose the functional tasks to practice based on the results of the measurement-based process. In addition, task practice sessions will be coached/guided by the therapist through a metacognitive strategy training process which is based on the Cognitive Orientation to Occupational Performance (CO-OP) approach aimed at enhancing self-management during home and community living tasks.

4.0 Study Endpoints

We will assess cognition (objective and subjective), functional task performance, activity participation, and psychosocial function with the following measures administered at pre- and post-treatment. Data will be analyzed to observe pre-to post- changes in average ratings of assessments listed in the Table.

Outcome	Instrument
Cognition: Objective	Montreal Cognitive Assessment (MoCA) is a 16-item objective cognitive screening measure. The maximum possible score = 30 points with higher scores indicating better cognition. Scores > 26 are considered unimpaired, scores < 23 indicate cognitive impairment[7]. Any necessary modifications for remote administration will be made according to guidelines provided on the official MoCA website (https://mocacognition.com/remote-moca-testing/). This may involve saving images of participants' paper-and-pencil responses using screen capture for the purposes of scoring.

Cognition: Subjective	NeuroQoL-Cognitive Function Short Form v.2.0[8]: 29-item subjective measure of cognitive function. This patient-reported outcome assesses perceived abilities in memory, attention, decision making, or in the application of such abilities to everyday tasks (e.g., planning, organizing, calculating, remembering, and learning) on a 5-item rating scale (1=cannot do to 5=no difficulty). The summed raw score will be converted into a normed T-score (mean=50, SD=10). Higher T-scores reflect better perceived cognitive function.
Functional Task Performance and Activity Participation: Ability for subjects to use the measurement-method to choose appropriately difficult tasks for at home self-directed task practice.	Patient Specific Functional Scale (PSFS)[9]: a patient-reported measure of task-goal identification and difficulty performing the task on a 0–10-point ordinal scale with higher ratings indicating greater satisfaction with task performance.[4, 5]
Functional Task Performance and Activity Participation: At home activity performance	Performance Quality Rating Scale (PQRS): The OT observes live performance (via the telerehabilitation video call) of one of the tasks not chosen on the PSFS. Subject's performance is rated by the OT on a 0-10-point ordinal scale with higher ratings indicating greater task performance skill.
Functional Task Performance and Activity Participation: Confidence in own at-home self-management skills	Stroke Self Efficacy Questionnaire (SSEQ)[10] is a 13-item patient self-report of their confidence (0–10-point Likert scale with higher numbers indicating greater confidence) doing at-home tasks such as using both hands to eat food or prepare a meal for oneself.
Psychosocial Function: Depression	Patient Health Questionnaire (PHQ-9)[11]: 9-item self-report measure of depression. Items query mood (feeling down, lack of interest), thoughts (guilt, suicidality), and physical symptoms (appetite, sleep, fatigue, concentration, restlessness). Each item is scored on a 4-point scale reflecting how often the symptom has occurred over the last 2 weeks (0=not at all, 3=nearly every day). Scores are summed (out of 27) and analyzed continuously or interpreted via thresholds: 0=no depression, 1-4=minimal depression, 5-9=mild depression, 10-14=moderate depression, 15-19=moderately severe depression, 20+: severe depression.
Psychosocial Function: Functional Impairment	Inventory of Psychosocial Functioning[12]: 80-item self-report measure of impairment in 7 psychosocial domains within the last 30 days: romantic relationships, family other than spouse/partner, work, friendships and socializing, parenting, education, and self-care. Participants rate the frequency of difficulty on each item on a 7-point scale (0=never, 6=always).
Psychosocial Function: Sleep disturbance and sleep related impairment	PROMIS Sleep Disturbance[13]: 8-item self-report of perceived difficulties falling and/or staying asleep. Items are rated on a 5-point rating scale (1=no problem, 5=very much a problem). The summed raw score will be converted into a normed T-score (mean=50, SD=10). Higher T-scores reflect more sleep disturbance.

5.0 Inclusion and Exclusion Criteria/ Study Population

Eligibility will be determined based on self-report or clinician assessment/determination, when indicated.

Inclusion Criteria

i. Have experienced ischemic or hemorrhagic stroke with resultant paresis of one arm/hand at least 30 days prior

ii. Adults ages 21 years or older

iii. Are able to speak and read English

iv. Have corrected vision to be able to read text on a screen

v. Have a device on which a telerehabilitation visit can be conducted (i.e., phone, tablet, or laptop) and a Wi-Fi connection or cellular service

vi. Able to participate in the study's assessment sessions as per the judgment of the licensed, experienced stroke telerehabilitation occupational therapist.

Exclusion Criteria

i. Have moderate-severe or severe aphasia.
ii. Have impaired decision making capacity as determined by the U-ARE protocol for assessing capacity to provide informed consent (described in Section 9.0).

Every effort will be made to recruit a diverse population. Stroke in South Carolina occurs to men and women of all ethnic and racial groups. We have no criteria that should exclude any person based on race, gender, or ethnic category. Hence will anticipate that our sample will be diverse.

6.0 Number of Subjects

N = 20

7.0 Setting

Procedures will primarily be conducted virtually via telephone and/or telehealth using an MUSC approved electronic platform (e.g., Doxy.me video visit) or in-person in MUSC research space. When virtual, the subject will be located in their home or work environment and the research team member will be located in the College of Health Professions Research Building at 77 President Street on the MUSC main campus or at an approved alternative work location.

8.0 Recruitment Methods

Participants with stroke will be recruited from 2 sources:

(1) The proposed research investigates stroke recovery; thus, it will be supported by the Clinical and Translation Tools and Resources (CTTR) Core of the NIH-funded Center of Biomedical Research Excellence (COBRE) in Stroke Recovery at MUSC. The CTTR Core facilitates subject recruitment through a bioinformatics-enabled database registry called RESTORE (all recruitment and database methods are approved under Pro#00037803). RESTORE currently contains contact information for ~1500 stroke survivors who have signed informed consent to be contacted for research participation and ongoing recruitment is expected to add 1-3 more subjects each week. The Co-I of this project (Dr. Woodbury) has successfully recruited >n=100 subjects for stroke rehabilitation studies using RESTORE in the past; thus, we are confident that recruitment goals for the present study will be met without difficulty.

(2) In addition, potential subjects will be identified from the existing Stroke Telerehabilitation - Occupational Therapy (Tele-OT) Quality Improvement program that is actively treating patients (funded by the Duke Endowment). The proposed project will recruit stroke survivors from the existing Tele-OT program in the following way: patients who are

referred to Stroke Tele-OT are phoned (as per usual practice) by Telerehab therapists to schedule the first telerehabilitation screen or visit. Information about the current study will be provided to the tele-therapists who will then provide information to the patient during this initial phone call. If a potential participant expresses interest, a team member of the current study will contact the potential participant to answer questions and schedule their first study visit at which informed consent will be obtained prior to starting study procedures.

Digital and physical recruitment materials: To aid in recruitment, we will disseminate a flyer designed for this study. For potential participants identified via either of the above methods, we will send a templated recruitment email that contains a description of the study, a blank copy of the consent form for their review, and our study team's contact information.

9.0 Consent Process

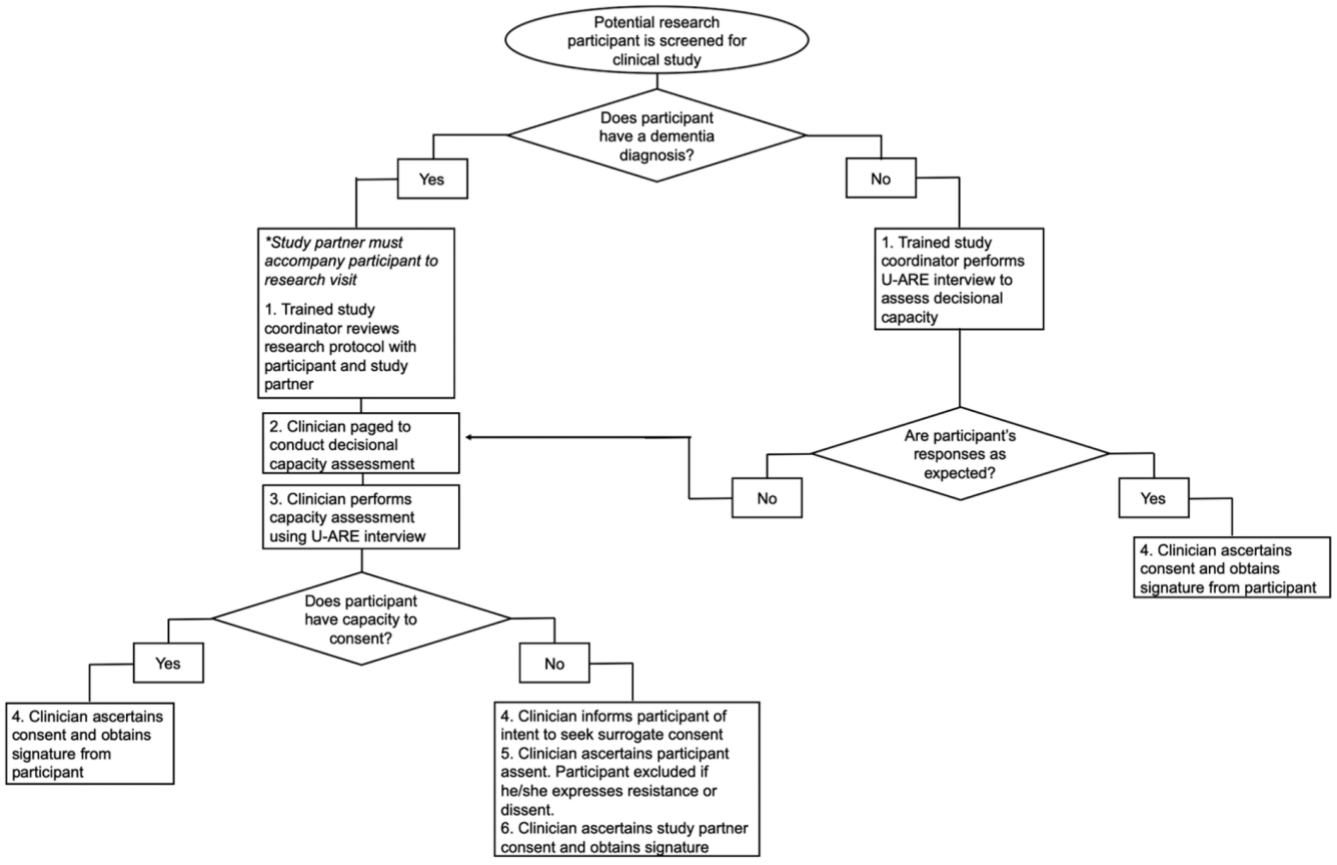
Informed Consent will occur during the PRE visit after the aphasia eligibility screening. Informed Consent will be obtained by approved study personnel in one of two ways depending on a potential participant's preference: via telehealth (eConsent) or in-person on MUSC campus in research-designated space.

- **e-Consent:** A link to the REDCap eConsent will be provided to the participant via a hyperlink (text or email). An approved member of the study team will review the consent document over the phone or via videoconferencing with the participant. Ample time will be provided for the potential participant to ask questions. The participant will electronically sign the eConsent and submit the REDCap survey. The study team member will then electronically sign the eConsent and print a PDF of the document. The signed PDF will be emailed or mailed to participants for their records. A downloaded signed e-consent form will also be stored securely in a locked cabinet in a locked office. In addition, the signed e-consent will be maintained electronically on REDCap.
- **In-person:** The consent process will take place in a private room when the potential participant comes to the Stroke Recovery Research Center, which will occur at a scheduled time agreed upon between the study personnel and the participant. The content of the consent will be verbally explained to the participant and the participant will be asked if he/she has questions and/or concerns. If the person requests a waiting period, then one will be given. If the person desires to consent immediately, then the person will provide consent immediately. No study procedures will occur until the informed consent is obtained.

Capacity to Consent: We will assess each participant's capacity to provide informed consent using the Understanding, Appreciation, Reasoning, and Expression (U-ARE[16]) protocol. The following procedures are in accordance with the U-ARE protocol's flowchart (See Figure 1). After reviewing the informed consent form, the trained study staff will perform the U-ARE interview to assess decisional capacity. This study will include individuals with aphasia (less than moderate/severe, per exclusion criterion *i*), which does not equate to an inability to provide informed consent[14]. For individuals with aphasia, the U-ARE items will be presented with appropriate communication supports (described in "Aphasia Supports" in Section 10.0). If the participant's responses are satisfactory, then the study staff will obtain the participant's signature on the ICF. If the participant's responses are not satisfactory, then the study staff will contact the PI or a designated clinician Co-Investigator to conduct the decisional capacity assessment (as specified in Figure 1). If the clinician determines that the participant has the

capacity to consent, the clinician will obtain the signature from the participant. If the clinician determines that the participant does not have the capacity to consent, then the clinician will inform the participant that they are no longer eligible to participate in this study. The study staff will continuously monitor participants for potential changes in decision-making capacity throughout the duration of their participation in the study. The U-ARE protocol will be re-administered if any member of the study team suspects changes in a subject's decision-making capacity.

Figure 1.



10.0 Study Design / Methods

Design: This is a quasi-experimental, single group pilot study that investigates the impact of integrating cognitive rehabilitation into an 8-week OT-led activity- and participation-based stroke telerehabilitation program. Participants will attend a total of 15 study visits over 10 weeks. A summary and timeline of procedures are outlined and described in the following table.

Visit Schedule: To accommodate participant preference/comfort and feasibility, we have designed the visit schedule to be flexible in the following ways:

- The PRE assessment visit will occur within 1-10 days prior Telerehab session 1 and the POST assessment visit will occur within 1-10 days after Telerehab session 13.

- Given the 2–3-hour length of the PRE session, the participant and therapist may decide to split the PRE procedures over 2 visits if the participant becomes fatigued or has other time constraints.
- We will make an effort to schedule telerehab visits on the days and times of the participants' choosing to the extent that the therapists' schedules permit.
- In extenuating circumstances that lead to cancelations/missed sessions (e.g., serious weather event, illness, holidays):
    - Telerehab sessions may extend into an additional week. This would make the intervention duration 9 weeks instead of 8 and the duration of full participation 11 weeks instead of 10.
    - Make-up telerehab sessions may be added to any intervention week.

Week	***Week 1***	***Weeks 2-3***	***Weeks 4-6***	***Weeks 7-9***	***Week 10***
Session	**PRE**	**1-4**	**5-10**	**11-13**	**POST**
Mode (session duration)	**Virtual (2-3 hrs)**	**Telerehab (45–75 min/session 2x/week)**	**Telerehab (45–75 min/ session 2x/week)**	**Telerehab (45–75 min/session 1x/week)**	**Virtual (2 hrs)**
Study Procedures	• Informed Consent • Collect emergency contact information • Administer characterization and outcome measures • Complete fall risk stratification • Telerehab Technology Training as needed • Brief initial introduction to the intervention approaches: cognitive rehabilitation and cognitive orientation to occupational performance (CO-OP) therapy approach *(described below)*	• Cognitive Rehabilitation 2x/week for 2 weeks. • At the end of the 4th session, develop a personalized, measurement-based home OT program *(described below) for use in subsequent sessions*	Cognitive Rehabilitation + OT with CO-OP Approach 2x/week for 3 weeks	OT with CO-OP Approach 1x/week for 3 weeks.	Administer outcome measures

Sessions 1-4 will provide cognitive rehabilitation strategy training focused on attention and executive function.
Sessions 5-10 will review cognitive rehabilitation strategy training and focus on the application of cognitive skills while engaging in OT for performance of home- and community-based activities.
Sessions 11-13 will emphasize the application of cognitive skills while engaging in OT for participation in home- and community-based activities.

Aphasia Supports: To accommodate individuals with aphasia, we will use supportive communication strategies to facilitate comprehension and understanding, as recommended by the study speech language pathologist (SLP) and in line with best practices for this population[15]. This may include using adaptive formatting (e.g., presenting small amounts of text at a time,

increasing spacing, using larger font), presented information verbally and/or visually, and allowing participants to respond verbally, in writing, or by pointing/selecting from a multiple-choice list.

Session "PRE": PRE-TREATMENT ASSESSMENTS

Aphasia Screening: Prior to consent, we will determine whether participants meet exclusion criterion *i* (moderate-severe or severe aphasia) by the following procedures:

1. The therapist will query whether the participant might have symptoms of aphasia: E.g., "Do you have any difficulty communicating with others since your stroke?"

If this question is endorsed or the therapist suspects aphasia based on their interactions, then:

2. The therapist will administer the Language Screening Test (LAST)[17] form A. This 15-item measure tests expressive and receptive language. We will make adaptations to accommodate remote administration when needed. Participants will be excluded from the study if they score:
    A. Less than 6/7 on the receptive index OR
    B. Less than 4/8 on the expression index OR
    C. A total score below 15/15 (but do not meet criteria A or B) and per clinical judgment:
        - For those meeting criterion C, the therapist conducting the assessment will consult with the study SLP to determine eligibility. If the therapist and SLP deem it necessary, the SLP will meet with the participant to do a more thorough evaluation of their aphasia and determine whether they should be included in the study.

Sample Characteristics: We will collect the following data at the initial visit that will be used to describe characteristics of the sample:

- Demographics: self-reported age, biological sex, gender, race, ethnicity, time since stroke, stroke location, pain, and stroke severity (NIH Stroke Scale).
- Technological Literacy via a questionnaire modified for stroke telerehabilitation[8]
- The Occupational Therapy Occupational Profile to qualitatively document aspects of the participant's context that impede/facilitate telerehabilitation including technology (internet, computer) and the physical and social home-context.
- We may also conduct medical chart review to collect the following information: stroke date, NIH Stroke Scale score, and discharge scores on stroke rehab assessments.

Outcome Measures: The research team member administering the outcome assessments will be trained on the administration and scoring of each assessment with standardized training videos, manuals, and appropriate supervision. We will assess cognition (objective and subjective), functional task performance, activity participation, and psychosocial function with the following measures administered at pre- and post-treatment unless otherwise specified:

Outcome Domain	Instrument
Cognition	MoCA
Cognition	NeuroQoL-Cognitive Function Short Form v.2.0
Functional Task Performance and Activity Participation	Patient Specific Functional Scale (PSFS)
Functional Task Performance and Activity Participation	Performance Quality Rating Scale (PQRS)[a]
Functional Task Performance and Activity Participation	Stroke Self Efficacy Questionnaire (SSEQ)
Psychosocial Function	Patient Health Questionnaire (PHQ-9)[b]
Psychosocial Function	Inventory of Psychosocial Functioning
Psychosocial Function	PROMIS Sleep Disturbance

[a]The PQRS will not be administered at the PRE and POST visits and instead will be administered at actual telerehab visits to more proximally assess function. Specifically, it will be administered at the beginning of the first telerehab visit (session 1), the beginning of the first visit with OT (session 5), and at the end of the last telerehab visit (session 13).

[b]The Columbia Suicide Severity Rating Scale (C-SSRS) will also be administered if suicidal ideation/intent is endorsed (as described in Section 12.0).

Telerehab Technology Training: Technology training and orientation will be provided as needed to participants to ensure understanding of the digital platform (Doxy.me). Study staff will provide written instructions via email, calendar invitation, or text message that include the webpage link to join the telerehab call with the therapist. Phone support may be provided as needed for clients who are unsuccessful with connecting at the scheduled appointment time. Study staff will orient the client to the video call interface and review how to turn the camera and microphone on and off to protect privacy, how to position themselves at the workspace in view of the camera to suitably participate in telerehab sessions, and how to contact the study staff or therapist if the video conference connection is lost.

Sessions 1-13: TELEREHABILITATION VISITS

Ensuring Safety During Telerehabilitation Sessions: At the beginning of each session, all participants will provide emergency information at the start of each telerehabilitation session as per standard tele- practices (i.e., address of current location, current phone number, phone number of emergency contact). The OT study staff will evaluate fall risk prior to beginning the intervention to guide parameters of the in-home telerehabilitation sessions to optimize patient safety.

Fall Risk Assessment: At the PRE session, the participant's risk for falling during an OT session will be determined as a combination of their cognitive and physical functioning based on information from established measures and the therapist's assessment/clinical judgment. If a participant is deemed a moderate or high fall risk (based on the stratification below or per the clinician's judgment), additional precautions will be taken to ensure safety. At-risk individuals will have to either 1) have a second person present for Telerehabilitation sessions (e.g., caregiver or trusted friend or family member) to assist with mobility during any dynamic standing activities and/or 2) complete the intervention in a seated position. This second person will be trained by the therapist to provide assistance to the participant during therapy activities that require standing or moving. If the second person is not available, the participant will be required to complete the intervention in a seated position. We will stratify participants into fall risk categories (see Table) using data from the following two measures according to the Table:

- Activities-Specific Balance Confidence (ABC) scale: a self-report questionnaire asking participants to rate their confidence in completing each of 16 activities without losing their balance or becoming unsteady from 0%=no confidence to 100% completely confident. Our risk stratification (see table) uses established cut points for the total ABC score[18].
- Montreal Cognitive Assessment (MoCA): The MoCA is administered as part of the study's outcome measures. We will use MoCA scores from the PRE assessment to stratify individuals into cognitively impaired (scores ≤23) and non-impaired.

	ABC Scale Score > 80 *(High functioning/ confidence in balance)*	ABC Scale Score = 50-80 *(Moderate functioning/ balance deficits)*	ABC Scale Score < 50 *(Low functioning/ balance deficits)*
MoCA Score 24 – 30 points (*Normal cognition / minimal cognitive impairment)*	Minimal Fall Risk.	Moderate Fall Risk	Severe Fall Risk
MoCA Score ≤ 23 points	Moderate Fall Risk	Severe Fall Risk	Severe Fall Risk

(Moderate to severe cognitive impairment)			

*Note that clinician's judgment of fall risk can supersede this stratification scheme. For example, if a participant stratified into the minimal risk category is deemed moderate/severe risk by the clinician's assessment then the above safety precautions will be implemented.

Cognitive Skills Interest Survey: We will collect information about participant's interest in the cognitive skills that will be covered during first cognitive rehab-focused visit (session 1) and the perceived usefulness of each cognitive skill at the last cognitive rehab-focused visit (session 4).

Measurement-based Home Program: In our past work, we conducted an item response theory Rasch analysis of existing data from n=512 subjects to whom all items of the Fugl-Meyer Upper Extremity Assessment (FMA-UE) had been administered. The analysis identified an item difficulty hierarchy in which items were arranged from easy-to-difficult on a "Keyform Recovery Map". Using a Recovery Map, the specific ability-level of an individual is located relative to items that are too easy, too difficult, or just-right for him/her to accomplish.

The location of the individual on the Recovery Map indicates optimal functional tasks for the client to practice. This is because the FMA-UE items reflect voluntary arm motions, hence the client's ability-level location (relative to item-difficulty) points to optimally difficult functional tasks for which the client has the just-right abilities. Moreover, the Recovery Map defines the functional tasks expected to be accomplished in the short term because they require movements that are slightly above the client's current ability-level. The Map also defines functional tasks expected to be accomplished in the longer term because the functional tasks require movements that are very difficult given the client's current ability-level. Hence, the use of the FMA-UE to define optimally difficult motions and functional tasks is an objective, measurement-based, method to design a home program specific to and personalized for each individual.

To design the measurement-based home program, the tele-FMA-UE will be administered to participants at the initial OT visit (session 4). The participant's ability-level will be located on the Recovery Map according to his/her scores on each item. In a collaborative discussion, the participant and therapist will identify functional tasks that are both optimally difficult (as per the measurement-based Map) and meaningful/motivating to the participant. These tasks will be assigned to the client as his/her home program, i.e., the optimally difficult tasks that the participant will practice in his/her home environment to drive his/her own post-stroke recovery. In this way, the measurement-based Mapping method identifies ***what*** specific tasks to do at-home. The tele-FMA-UE may be repeated at subsequent OT sessions and post-treatment assessment to monitor progress.

Cognitive Orientation to Occupational Performance (CO-OP) is a metacognitive strategy-training approach to teach participants ***how*** to successfully use the paretic arm for the tasks identified with the measurement-based method described above. CO-OP is emerging as an effective method to improve stroke survivors' skills to self-manage daily life during home and community living tasks.[11-15] In this approach, with guidance/coaching from an occupational therapist, participants learn to analyze their own performance and develop personalized strategies to overcome task performance challenges with the overall goal of generalizing skills into life situations when a therapist is not present. The CO-OP approach integrates principles of learning theory with motor skill acquisition. The participant is viewed as a "learner" and the therapist is viewed as a "facilitator". The clinician facilitates the participant's guided discovery of

errors and development of cognitive strategies to attain meaningful occupational goals and performance improvements using a “Goal-Plan-Do-Check” framework.

During a CO-OP task-practice session, the participant may be seated or standing at a table with the task objects arrayed within the reachable workspace. The therapist asks the client to identify the task goal (e.g., eating with a spoon), and the client is asked to explain how they plan to approach the activity using guided questions as needed (e.g., explaining movement strategies, set-up of the activity, key performance areas, etc.). The therapist intermittently provides verbal coaching and feedback such as “How do you think it is going?” and/or, “Can you tell me what is going well and what is not going well?” to guide the client through the selected task. Guided-questioning intervals will be adjusted according to patient success with the selected task, allowing the client time to problem-solve independently through errors depending on their level of understanding. Upon completion of the task, the therapist will ask the participant to “Check” their performance, asking questions such as, “How did you do?”, or “Is there anything you want to change the next time you try this task?”. The client will then engage in a discussion about his/her performance on the task according to the goals set prior to the start of the activity, (e.g., “I had trouble keeping my shoulder down while trying to bring the spoon to my mouth.”) The activity will be repeated as necessary to confirm understanding and integration of new strategies.

Session “POST”: POST-TREATMENT ASSESSMENTS

Outcome Measures: We will repeat the same measures administered at pre-treatment to assess cognition (objective and subjective), functional task performance, activity participation, and psychosocial function:

Outcome Domain	Instrument
Cognition	MoCA
Cognition	NeuroQoL-Cognitive Function Short Form v.2.0
Functional Task Performance and Activity Participation	Patient Specific Functional Scale (PSFS)
Functional Task Performance and Activity Participation	Performance Quality Rating Scale (PQRS)[a]
Functional Task Performance and Activity Participation	Stroke Self Efficacy Questionnaire (SSEQ)
Psychosocial Function	Patient Health Questionnaire (PHQ-9)[b]
Psychosocial Function	Inventory of Psychosocial Functioning
Psychosocial Function	PROMIS Sleep Disturbance

[a]The PQRS will not be administered at the PRE and POST visits and instead will be administered at actual telerehab visits to more proximally assess function. Specifically, it will be administered at the beginning of the first telerehab visit (session 1), the beginning of the first visit with OT (session 5), and at the end of the last telerehab visit (session 13).
[b]The Columbia Suicide Severity Rating Scale (C-SSRS) will also be administered if suicidal ideation/intent is endorsed (as described in Section 12.0).

Telerehab Experience Survey: At the POST visit, participants will complete two brief surveys regarding their experiences of completing the telerehabilitation program, the Acceptability of Intervention Measure (AIM) and the Intervention Appropriateness Measure (IAM)[19]. They will also have the option to provide narrative, qualitative responses about what they liked and did not like about the program. The survey will be administered via Redcap.

11.0 Data Management

Recruitment Data: Recruitment records will be housed in REDCap. Only IRB-approved study personnel will have access to the REDCap database while actively enrolling for the study.

Data Analysis: Data from the prospective sample (n=20) will be used to calculate descriptive statistics of all outcome measures collected prior to (pre-treatment) and immediately following (post-treatment) the intervention and the corresponding change scores. The preliminary effect sizes of the proposed intervention will be generated by evaluating 1) change in each outcome measure from pre- to post-treatment and 2) the associations between changes in cognitive measures and changes in the participation and psychosocial function measures. To explore the potential additive benefit of cognitive priming, we will compare change in the participation measures between the prospective sample (n=20) and historical data (n=30) from stroke survivors who have completed the telerehabilitation program without the cognitive rehabilitation primer component.

Confidentiality: All data except for the consent forms and HIPPA forms will be coded at the time of data recording. All electronic data will be stored in a password-protected research server that is accessible to IRB-approved study personnel only. All paper data with personally identifiable information (e.g., the consent forms) will be stored in a key-locked cabinet in a key-locked room that is accessible to IRB-approved study personnel only. Other paper data without personally identifiable information including testing sheets documenting testing sequences and notes will also be stored in a cabinet in a key-locked room that is accessible to IRB-approved study personnel only.

Data sharing: Only de-identified coded data will be reported and/or shared with the public and other investigators in publications, in ClinicalTrials.gov, or via data depository.

12.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

The data and safety monitoring plan will include an internal Data Safety Monitoring Committee (DSMC) and the Institutional IRB. The purpose of the DSMC and IRB are to ensure the safety of participants and the validity and integrity of the data.

Data Safety Monitoring Committee (DSMC). The internal DSMC will consist of the PI and Co-Investigators on the proposal. The functions of the DSMC will include: 1) providing scientific oversight; 2) reviewing all adverse effects or complications related to the study; 3) monitoring enrollment; 4) reviewing summary reports relating to compliance with protocol requirements; and 5) providing advice on resource allocation. The DSMC will meet quarterly, remotely or in-person. The recommendations of the DSMC will be reviewed and the PI will take appropriate corrective actions as needed.

Reporting of safety data: All serious adverse events will be reported to the IRB as they occur. Summative safety data will be reported to ClinicalTrials.gov and in publications. As such, we will register this study in ClinicalTrials.gov as soon as the study commences and report results including all adverse events as soon as the study is completed following the guidelines. To protect participants' confidentiality, personally identifiable information will not be used for reporting. Only de-identified or aggregated data will be used for reporting.

PHI: Study participants will receive a study-specific ID code. All study information will utilize only the study ID code, not PHI. PHI will be stored in a password protected site on the MUSC network. The master list that links the study ID to PHI will be stored separately from other study data in a password protected site on the MUSC network to minimize the potential for loss of confidentiality

if study documents are lost or compromised. Paper-copy PHI data will be stored in a locked storage cabinet within a locked office.

Suicidal Intent: Suicidal intent will be assessed during the pre-treatment and post-treatment assessment visits via item 9 of the PHQ-9 ("Thoughts that you would be better off dead, or of hurting yourself"). Participants who endorse a rating > 0 ("not at all") on this item and verbally endorse suicidal ideation upon query will then be assessed using the Columbia Suicide Severity Rating Scale (C-SSRS). The research team is comprised of licensed, experienced occupational therapists and clinical psychologists, all of whom will have training in suicide risk assessment. Consistent with the triage points determined by the scale authors, any positive endorsement to items 3 – 6 on the C-SSRS will necessitate completion of a safety plan (which will be sent to them via email once completed) and consultation with the PI or a designated clinician Co-Investigator (Dr. McTeague). Any positive endorsement of items 4 – 6, and participation may be discontinued based on clinician Co-I judgment. Depending upon the follow-up to endorsement of item 3 (passive ideation), participation may also be discontinued. Any participant endorsing items 4-6 will be referred to immediate consultation with the PI or a designated clinician Co-Investigator (Dr. McTeague) who will discuss a safety plan and provided appropriate referrals and follow-up contact to facilitate engagement in care. In the case of imminent suicidal intent or danger, a research team member will remain in contact with the participant while calling 911 (providing the dispatch with the participant's current location). A research team member will also contact the participant's emergency contact.

13.0 Withdrawal of Subjects

Subjects who repeatedly fail to attend scheduled visits or do not complete the 10-week intervention within 12 weeks may be withdrawn by the investigator. Subjects who are or become medically unstable may be withdrawn by the investigator.

A subject may choose to stop the project at any point in time. He/she may choose to reschedule or stop participation altogether. For those who are withdrawn by the investigator, or those who voluntarily withdraw from the study, their data collected up to that point may be used by the investigator.

14.0 Risks to Subjects

There is a minor risk of mental and/or physical fatigue from engaging in the cognitive rehabilitation and occupational therapy rehabilitation intervention. There is also a risk of falling during the occupational therapy sessions. There is a risk that stroke survivors may experience sadness, fear, or anger if they have difficulty with the assessments or intervention because they may develop a greater realization of their deficits. It is also possible that the task-practice sessions result in temporary muscle soreness or fatigue. These risks to participants are no more than a usual-care stroke rehabilitation assessment and/or intervention session.

There is a risk of a loss of confidentiality of personal information that is used in this study although researchers will take appropriate steps to protect any information collected about the participants.

15.0 Potential Benefits to Subjects or Others

There may be no benefit from participating in this study. The potential benefit is that the telerehabilitation program (cognitive rehabilitation in combination with measurement-based task practice with metacognitive strategy training) will promote participants' recovery of paretic arm/hand function, although this cannot be guaranteed. The knowledge regarding the potential of using this measurement-based method to improve function and activities of daily living for people who had a stroke may benefit stroke survivors in general.

16.0 Sharing of Results with Subjects

If a subject requests a copy of the assessment results, a printed copy of the results will be mailed or emailed to him/her.

If the subject agrees, the data collected and generated from this study will be shared to the Registry for Stroke Recovery (RESTORE-Pro#00037803) by the subject's registry ID. Sharing data from this study with the registry will allow for more targeted recruitment efforts in the future and allow researchers at MUSC to have a more complete registry with key stroke recovery elements including common data and physical function characteristics that are applicable to multiple studies. MUSC researchers and collaborating facilities will be able to query data sets to learn more about recovery of subjects after their stroke through institutionally managed secure servers that will assure HIPAA privacy and security compliance.

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