Implementation of Exergame Telehealth in Subjective Cognitive Decline

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ABSTRACT

Background: The purpose of this pilot study was to evaluate the feasibility and safety of a synchronous, remotely delivered, simultaneous aerobic exercise (AEx) and cognitive training program (Exergame) via BrainFitRx® in persons at risk for Alzheimer's disease (AD) dementia.

Methods: In this pilot study, we employed a randomized controlled trial design in which participants were randomized to 1 of 3 groups: Exergame, AEx only, or stretching control on a 2:1:1 allocation ratio, 3 times a week for 12 weeks. Sessions were supervised in a synchronous audiovisual telehealth format by a clinical exercise physiologist. Feasibility and safety outcomes were assessed as session attendance, intensity adherence, and study-related adverse events. Usability for the Exergame was assessed by the Systems Usability Survey.

Results: The average age of the study sample (n = 39) was 74.6 ± 7.2 years old with 17.7 ± 2.3 years of education and 69.0% female. Overall participants in the Exergame and AEx groups attended on average 83.8% of possible sessions over the course of the 12-week study (85.6% attendance overall). Attendance was significantly higher for the AEx group (P = 0.02). Of the total training sessions completed collectively, 87.7% of sessions achieved the prescribed moderate intensity rating of perceived exertion targets (84.3% and 94.9% of sessions, respectively, for the Exergame and AEx groups). Overall, there were 2 study-related adverse events, both in the Exergames group. The Systems Usability Survey score was considered acceptable for the BrainFitRx.

Conclusions: In this study, we provide preliminary evidence of the feasibility of a simultaneous AEx + cognitive training (Exergame) program delivered through a synchronous telehealth format.

Keywords: aerobic exercise, cognitive training, audiovisual rehabilitation

INTRODUCTION

Currently, the population of people 65 years and older is approximately 55.9 million, representing 17.1% of the total US population; it is expected to grow to 80.8 million by 2040 (1). The increasing aging population is a primary factor that is driving the growing number of older adults suffering from Alzheimer's disease (AD), a disease that currently affects 6.5 million Americans (2). Currently, interventions aimed at later clinical phases of AD are ineffective or have shown only modest benefits (3). In contrast, the preclinical state (i.e., subjective cognitive decline [SCD]) offers a therapeutic window into where interventions have strong potential to prevent or delay progression to AD dementia (4,5). Aerobic exercise (AEx) and cognitive training are 2 potential disease-modifying interventions through the induction of brain plasticity and attenuation of AD neurodegeneration (6–8). Given that AEx and cognitive training work through discrete neuronal mechanisms, combined AEx and cognitive training might have a synergistic and superior effect on cognition compared with either intervention alone (9). Despite the growing evidence regarding the therapeutic effects of combined AEx and cognitive training, implementation of such rehabilitation programs that focus on AD prevention and management are lacking (10). This aligns with the poor uptake and adherence to rehabilitation programs in general (11).

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Recently, advancements in technology have allowed for home-based telehealth/telerehabilitation interventions to be used as a supplement or replacement to conventional rehabilitation programs (12–20). Individuals in these home-based programs can do so under varying levels of supervision from trained professionals with some programs having direct supervision (i.e., synchronous) and others having little to no supervision at all (i.e., asynchronous). Although telehealth/telerehabilitation is a growing form of therapy (12–20), it has classically been studied in the context of exercise therapy and not in the context of a combination therapy (with cognitive training).

The primary aim of this study was to assess the feasibility and safety of a synchronous, remotely delivered, concurrent cognitive training and AEx (Exergame) program (BrainFitRx®) compared with AEx alone in participants with SCD. We expected that the synchronous, telehealth format would enhance program attendance and not impede participants' ability to achieve targets of moderate intensity as outlined by the American College of Sports Medicine (ACSM) (21). Specifically, we anticipated that session attendance would exceed 80%, and intensity targets would be achieved in ≥80% of attended sessions in both active groups. Threshold targets were based on previous telerehabilitation pilot studies in neurological conditions (22). Secondly, we hypothesized that, collectively, the synchronous, telehealth program would be safely conducted as indicated by the low incidence of adverse events (AEs). Lastly, in the Exergame group, we projected that participants would report an acceptable level of usability (23,24) as indicated by a score ≥70% on the Systems Usability Survey (SUS) (23).

METHODS

Design

In this pilot randomized controlled trial, we used a 3-parallel-groups design and randomized 39 participants to 3-month supervised Exergame, AEx (cycling) only, or stretching control groups on a 2:1:1 allocation ratio. Randomization was stratified by age (<75 and ≥75 years) using random permuted blocks of 4 and 8. Allocation was concealed from all investigators and data collectors, except for a statistician who generated the randomization sequence. The randomization sequence was concealed electronically through the Research Electronic Data Capture (REDCap) randomization module. Informed consent was received from participants. This trial was approved by the University of Minnesota Institutional Review Board (IRB: # 1610M98324). Details of the trial protocol (NCT04311736) have been previously published (25).

Participants

To be enrolled in the study, participants had to be English-speaking, older (>65 years), community-dwelling adults with SCD (indicated by answering *yes* to both, "Do you perceive memory or cognitive difficulties?" and "In the last 2 years, has your cognition or memory declined?"). Persons were excluded if they were physically active (i.e., ≥3 days per week for ≥30 minutes per bout). Other exclusionary criteria included objective cognitive decline (a score of <26/41 on the 11-element Telephone Instrument for Cognitive Status [TICS]) (26) or diagnosis of mild cognitive impairment or dementia. In addition, persons who had evidence that chemical dependency, neurological condition, or an uncontrolled or major psychiatric disorder were the likely cause of SCD were excluded. Uncontrolled or major psychiatric disorders were defined by any of the following: diagnosis from participants' physician, Geriatric Depression Scale Short Form (GDS-SF) score > 5 (27), Geriatric Anxiety Scale-10 (GAS-10) score ≥ 12 (28), or Beck's Anxiety Inventory (BAI) score ≥ 36 (29). Lastly, persons with an ACSM exercise contraindication (21) were excluded. The eligibility criteria, specific for SCD, aligns with research criteria for SCD outlined by Jessen et al. (30).

Procedures

Recruitment

Primary recruitment tools used for the Exergames Study included use of fliers and brochures as well as online recruitment tools. Fliers and brochures were placed in community centers, clinics, and fitness and rehabilitation facilities. Online recruiting efforts included targeted advertisements through Facebook and through targeted e-mail blasts with the University of Minnesota's University Retirees Volunteer Center.

Screening

Screenings were performed either via phone (screening 1 [S1]) or virtually over Zoom® (screening 2 [S2]). In the S1 phase, participants were screened for their SCD status (which included the administration of the TICS) and for contraindications to exercise. Consenting was carried out remotely at the second screening (S2) visit via e-Consent and Zoom, as e-Consent was administered through REDCap, a Web-based, data collection system that has been validated as compliant with FDA 21 CFR Part 11 (31,32). Upon completion of the virtual e-Consent, participants were e-mailed links for completing REDCap surveys that further accessed SCD status, affective conditions, and full health and medical history with the purpose of screening for exclusionary criteria specific to the likely cause of SCD. Affective and SCD symptoms were assessed by the GDS-SF (27), GAS-10 (28), BAI (29), and SCD My-Cog (33). After completion of the virtual S2 visit, study staff faxed each participant's primary care provider, which served to inform them about their study participation and requested their written clearance. Primary care provider clearance (screening 3 [S3]) was sought to further ensure that (a) no exercise contraindications were present and (b) causes of SCD were not attributed to (i) major psychological disorder, (ii) metabolic disorder, or (iii) induced by medication or chemical dependency. Upon completion of the screenings, eligible participants were scheduled for baseline data collection. All data collections pertaining to outcome assessments for the Exergames Study were performed on the university campus.

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Intervention

After baseline data collection and randomization, all participants completed a 1-session onboarding period (familiarization) in which the study interventionist/therapist (i.e., clinical exercise physiologist) delivered all necessary equipment (recumbent cycle, pulse oximeter, automated blood pressure monitor, etc.) to the participant's home. During this in-person visit, the interventionist reviewed the program, how to use equipment (including Zoom), directly supervised the first session to ensure participant understanding and fidelity of their specific intervention, and watched for potential signs of AEs to exercise. Thereafter, each of the 3 groups were encouraged to attend weekly sessions (frequency = 3) facilitated by the clinical exercise physiologist using a synchronous telehealth (audiovisual) format for 3 months (36 total sessions). All sessions were facilitated by clinical exercise physiologists using a synchronous, telehealth format, supervised over video with Zoom. Sessions were conducted using a 1:1 or 1:2 therapist to participant ratio; however, there was no mismatching of groups when 2 participants attended a session together. During sessions, heart rate (HR; monitored by either a HR monitor [Polar RS 400; Kempele, Finland] or a pulse oximeter [SantaMedical Generation 2; Tustin, CA]) and rating of perceived exertion (RPE) was assessed every 5 minutes. Participants were prompted by the therapist to read their respective device and communicate verbally to the therapist who subsequently recorded. Blood pressure was measured before and after exercise. Additionally, at the halfway point of the session, participants were instructed to assess their blood pressure with the automated blood pressure cuff (OMRON Gold; Kyoto, Japan) and communicate the reading to the therapist for documentation.

AEx

The AEx cycling intervention was conducted on recumbent stationary cycles (Exerpeutic 900SL; Industry, CA) at moderate intensity. Because of the absence of a baseline cycling-based cardiopulmonary exercise test and the potential influence of cardiovascular disease (and medications [i.e., beta blockers]) on the accuracy of prediction equations for establishing HR ranges [i.e., "HRmax" and "heart rate reserve"], RPE was used as the primary method for guiding exercise intensity and targeted 11–14 on the Borg Category Ratio-15 RPE Scale (34). As a secondary measure of intensity, HR was measured and targeted a resting HR +20–30/30–40 (35). Cycling was progressed weekly (every 3 sessions), alternating between intensity and duration. Week 1 exercise prescription was an RPE of 11–12 (resting HR +20–30) for 30–35 minutes, which was then increased by 1 point on Borg (Week 2) and then by 5 minutes (Week 3) until the individual was able to exercise at RPE 12–14 (resting HR +30–40) for 50 minutes a session over time. Each session included a 5-minute warmup and cooldown in addition to the prescribed exercise duration.

Exergame

Participants in the Exergame group performed aerobic cycling as described in the AEx protocol while simultaneously engaging in cognitive training for the duration of cycling. Cognitive training was matched to the cycling duration. The Exergame (BrainFitRx; Moai Technologies, L.L.C.; Maple Grove, MN) was housed on either an Apple TV (Apple Inc.; Cupertino, CA; Figure 1a) or iPads (Apple Inc.; Cupertino, CA) that were suspended off the cycle ergometer through a tablet holder. Participants controlled navigation through the Exergame with an Xbox-360 controller (Microsoft Corporation; Redmond, WA). The Exergame included 10 levels of difficulty with 9–10 different cognitive task (game) scenarios in the context of 3 virtual worlds (environments): City, Underwater World, and Wild West. In each of the environments, the participant was to follow directions and navigate to a destination where the cognitive task was to be performed (Figure 1b). Cognitive tasks in the Exergame reflect tasks that are considered to have high ecological validity (36,37) and are specific to the environment. For instance, cognitive tasks in the City setting include:

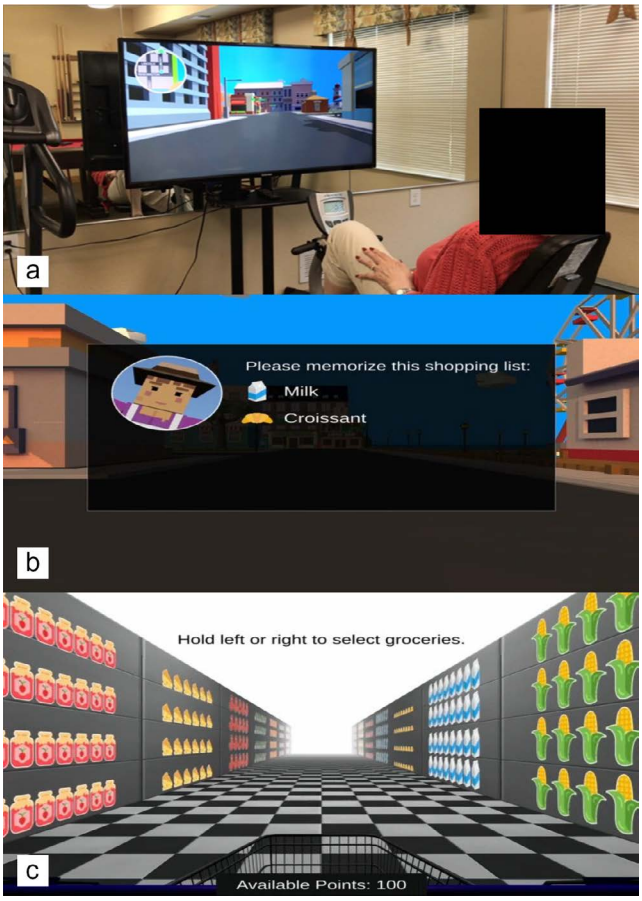

FIGURE 1. (a) Pilot Exergame system (BrainFitRx) setup with Apple TV set-top and HDTV display. The Exergame system was also modified to be housed on iPads that were suspended off the cycle ergometer through a gooseneck tablet holder (not pictured). Participants controlled navigation through the Exergame with an Xbox-360 controller. Virtual cognitive tasks: The grocery shopping cognitive task, as part of the "Small-Town Downtown" environment, challenges executive function, attention, and working memory cognitive domains. Once participants approach the destination (grocery store), (b) they are asked to memorize the shopping list and (c) then complete shopping.

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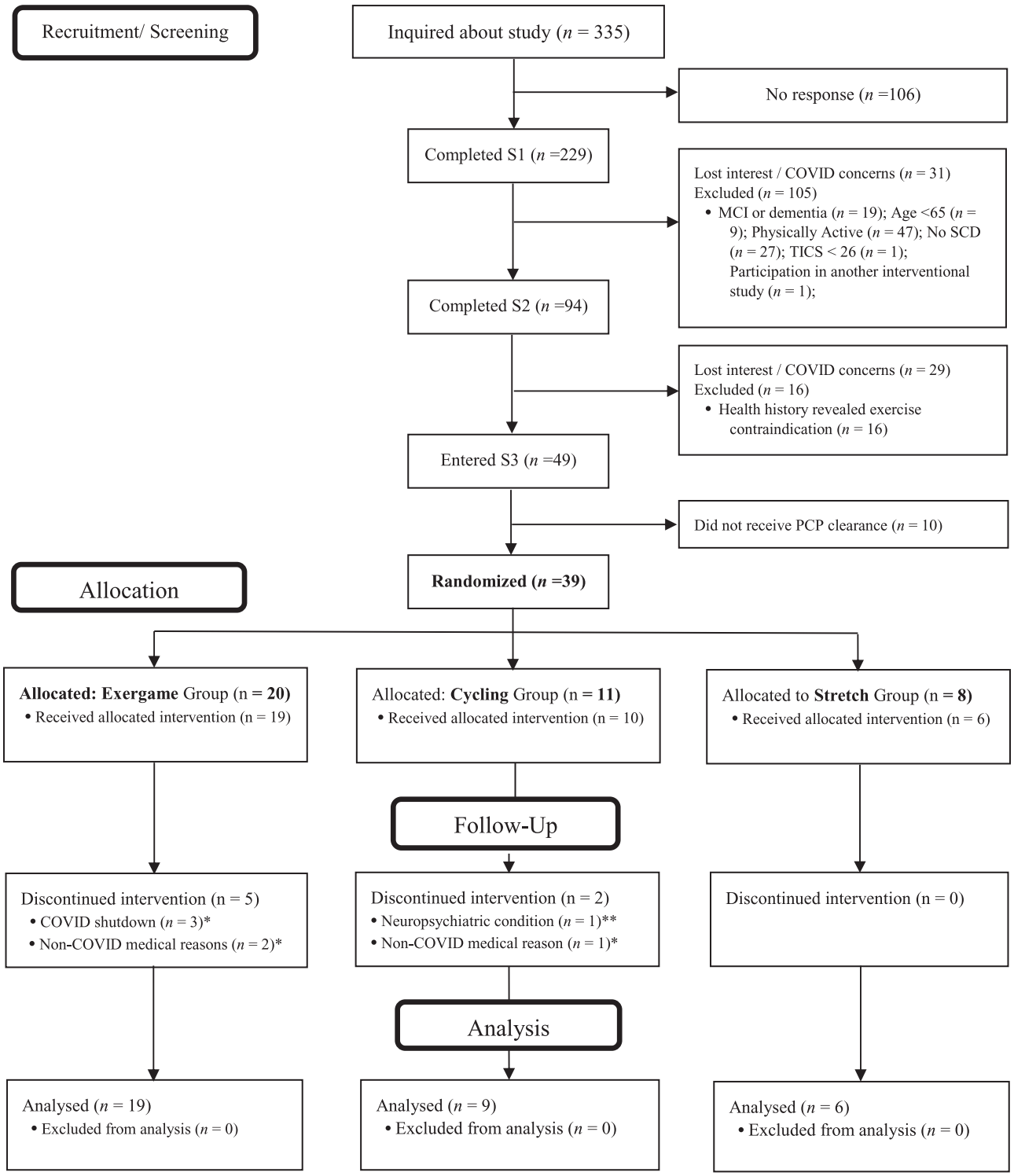

FIGURE 2. The Exergames Study consort diagram. S1 = screening 1; S2 = screening 2; S3 = screening 3; MCI = mild cognitive impairment; SCD = subjective cognitive decline; TICS = Telephone Instrument for Cognitive Status. Four participants did not start interventions (2 did not like the group assignment [stretch, cycling], 2 had unexpected family obligations due to COVID pandemic causing time restraints). *All started interventions but had to stop. All attendance (adherence) in these participants reflects number of possible sessions that could have been attended before discontinuation. **Participant had underlying and undiagnosed neuropsychiatric condition that was then diagnosed after completion of session 1. This individual was not included in the analysis. All others that discontinued intervention were included in the analysis with adjustments for the attendance metric.

(a) visiting the post office to mail a letter (post office), (b) sorting books at the library (book sorting), and (c) going shopping at the grocery store (grocery shopping; Figure 1c). A complete list of cognitive tasks (and associated cognitive domains/skills tasked) for City and Underwater World are found in Table 1. The cognitive training was progressed at the individual level

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TABLE 1. Cognitive training components of the Exergame program (BrainFitRx).

Cognitive Tasks	Cognitive Domains/Skills Exercised									
	Executive Function	Attention	Multiple Task Sharing	Stimulus Selection	Working Memory	Rule/ Concept Acquisition	Cognitive Strategy Flexibility	Planning	Mental Rotation	Decision Making
Grocery shopping[a]	X	X		X	X					
Flower shopping[a]	X	X		X	X					
Dish sorting[a]	X	X		X	X	X	X			
Dish sorting—advanced	X	X		X	X	X	X			
Book sorting[a]	X	X		X	X	X				
Book sorting—advanced[a]	X	X		X	X	X	X			
Post office[a]	X				X					
Museum maze[a]	X	X	X	X						
Mineral collecting[a]				X					X	
Treasure collector[b]	X	X		X	X					
Photographer[b]	X	X	X	X	X	X	X			
Feed the fish[b]	X	X		X	X	X				
Junk yard navigation[b]	X	X		X					X	
Shell sorting[b]	X	X		X	X	X	X			
Shell sorting—advanced[b]	X	X		X	X	X	X			
Cave maze[b]	X	X	X							
Recovering valuables[b]	X	X							X	
Lost pyramid[b]	X	X		X	X					
Oxygen monitoring[b]	X	X	X	X	X		X	X		X
Navigation by landmark[c]	X	X		X	X		X	X		X
Navigation by inset map[c]	X	X		X	X			X	X	X

[a]Cognitive games found within the City setting
[b]Cognitive games found within the Ocean Floor setting
[c]Found in all settings

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TABLE 2. Baseline demographic and clinical characteristics of each group.[a]

Variables	Exergame (n = 20)	AEx (n = 11)	Stretching (n = 8)
Age (y), mean ± SD	74.7 ± 7.6	75.8 ± 8.9	72.6 ± 4.3
Age of SCD onset (y), mean ± SD	69.9 ± 7.4	71.4 ± 10.6	67.3 ± 6.2
SCD total score (MyCog), mean ± SD	6.1 ± 4.1	9.0 ± 3.5	8.1 ± 2.5
TICS, mean ± SD	35.1 ± 2.2	34.3 ± 1.3	33.0 ± 3.1
GDS, mean ± SD	2.45 ± 2.28	1.60 ± 1.35	2.38 ± 1.76
GAS-10, mean ± SD	2.50 ± 2.16	3.40 ± 1.78	2.63 ± 2.07
BAI, mean ± SD	2.70 ± 2.27	3.30 ± 3.71	3.13 ± 3.23
Education (y), mean ± SD	17.5 ± 2.8	17.8 ± 1.7	17.9 ± 2.0
No. medications, mean ± SD	4.2 ± 2.9	2.5 ± 1.3	3.3 ± 1.8
Sex, female (%)	11 (55.0)	10 (90.1)	6 (75.0)
Race, white (%)	20 (100)	10 (90.1)	8 (100)
SCD onset in past 5 y (%)	17 (85.0)	6 (54.5)	6 (75.0)
SCD predominant in memory domain (%)	5 (25.0)	4 (36.4)	2 (25.0)
SCD perceived worse than others (%)	4 (20.0)	1 (9.0)	2 (25.0)
SCD concern enough to ask provider (%)	9 (45.0)	3 (27.2)	4 (50.0)
Depression (%)	13 (65.0)	5 (45.5)	4 (50.0)
Heart disease (%)	8 (40.0)	3 (27.3)	1 (12.5)
TIA/stroke (%)	1 (5.0)	2 18.2)	-
Anxiety (%)	4 (20.0)	5 (45.5)	2 (25.0)
Depression or anxiety medication (%)	5 (25.0)	3 (27.3)	3 (37.5)
AD medication (%)	-	-	-

AD = Alzheimer's disease; AEx = aerobic exercise; BAI = Beck's Anxiety Inventory; GAS-10 = Geriatric Anxiety Scale (10-item version); GDS = Geriatric Depression Scale (short form); MyCog = SCD Questionnaire Part I; SCD = subjective cognitive decline; TIA = transient ischemic attack; TICS = Telephone Instrument for Cognitive Status

[a]No significant differences for demographic or clinical characteristics between groups

based on performance in a specific cognitive game/task. Upon achieving a threshold score for a various cognitive task, the participant advanced a level (i.e., difficulty of the task increased) in the next session. However, advancing a level on 1 task did not automatically advance the participant a level on the rest of the 9 cognitive tasks).

Attention Control

Participants in the attention control group performed passive stretching exercise that we have previously tested (25). Sessions were matched by duration to the AEx and Exergame groups and were prescribed as light-intensity (RPE ≤ 9) stretching exercises (seated movements and static stretches) that induce no changes in aerobic fitness (25).

Main Outcomes and Measures

Feasibility outcomes included session attendance, intensity adherence, and usability of the BrainFitRx. Safety was measured as the number of study-related AEs and their severity.

Feasibility of Synchronous AEx-Based Telehealth

Session attendance was defined as the total number of sessions attended of 36 possible sessions to give 1 quantitative metric of intervention feasibility. For participants who were amid their respective program at the time of COVID shutdown or had medical reason that required discontinuation of the program, attendance (%) was adjusted to reflect number of sessions attended of the possible number of sessions available to date. Secondly, in each session, RPE and HR that were recorded over each 5-minute interval of exercise were averaged for each participant. Cumulated averages for RPE were quantified and compared with published ACSM exercise prescription guidelines (21) for moderate intensity and used to quantify intensity adherence. Participant adherence (attendance) was considered acceptable and optimal at thresholds of 60% and at least 80%, respectively, based on previous telerehabilitation research (22). Likewise, if 60%–79% of attended sessions achieved RPE targets, this was considered an acceptable threshold for intensity adherence, while ≥80% represented an optimal threshold (22).

Safety

Data regarding number and type AEs were tracked throughout the study and used as a surrogate of safety-related outcomes. Nonstudy-related AEs were categorized as either *clearly not related to the study* or *doubtfully related to the study*.

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Study-related AEs were categorized as *possibly*, *likely*, or *clearly* related to the study. The type of AE (cardiac, limb, musculoskeletal, metabolic, other) and incidence were recorded. Lastly, the severity of the AE was categorized as (a) minor (no treatment required), (b) moderate (resolved with treatment), and (c) serious (resulted in inability to carry on normal activities or ongoing medical treatment was still required). All AEs were assessed and graded by study investigators. Study-related AEs per number of training hours were calculated for each group.

Usability

After completion of the 12-week intervention period, participants randomized to the Exergame group were administered the SUS to evaluate the BrainFitRx. The SUS (23) is composed of 10 questions scored on a 5-point Likert scale and employs the following scoring: 1 = *strongly disagree*, 2 = *disagree*, 3 = *neither agree or disagree*, 4 = *agree*, and 5 = *strongly agree*. The survey was scored according to standardized instructions. Total scores range from 0 to 100. The SUS is widely considered a reliable and valid tool, providing a global view of subjective usability (23,24). A score of ≥70 is needed for an acceptable solution, <50 is unacceptable, and 50–69 is marginally acceptable (24).

Statistical Analysis

Means and standard deviations were quantified for feasibility measures (i.e., adherence [attendance and intensity compliance], and usability of the BrainFitRx), while AEs were expressed as frequency (percent). Comparisons for attendance and exercise duration were made across groups by 1-way analysis of variance (ANOVA). Between-groups comparisons (Exergames versus AEx only) for intensity compliance were made by independent samples *t* test. Significance was set at $P = 0.05$. All data were analyzed using SPSS version 28.0 (IBM Corp.; Armonk, NY).

RESULTS

The average age of the study sample (n = 39) was 74.6 ± 7.4 years, and 69% were female (Figure 2). Their average TICS score was 34.4 ± 2.4. Ninety-seven percent were non-Hispanic white with an average 17.7 ± 2.3 years of education (Table 2).

Feasibility

Overall adherence in the Exergames Study was 85.6% over the course of the 12-week intervention. However, attendance was significantly higher for the AEx group ($P = 0.02$) than the Exergame group. Of the total training sessions completed collectively by the Exergame and AEx groups, 87.7% of sessions achieved the prescribed RPE targets (84.3% and 94.9% of sessions, respectively, for the Exergame and AEx groups). Collectively, for the Exergame and AEx groups, the average RPE was 12.8 ± 0.6, with no significant differences between groups ($P = 0.14$; Table 3).

Safety

Overall, there were 2 study-related (likely caused by intervention) AEs in the training hours that both occurred in the Exergame group (Table 4), which equated to 0.004 AEs per training hour.

Usability

The mean SUS score for the BrainFitRx was 75.2 ± 16.8, with scores ranging from 45 to 95. Overall, 15 participants (75%) had scores ≥70 (acceptable), 3 participants (15%) had scores 50–69 (marginally acceptable), and 2 participants (10%) had scores <50 (unacceptable). Interestingly, concerning the usability of the Exergame in terms of user-friendliness (items 2–4 and 8), 80% of the participants answered agree or strongly agree.

DISCUSSION

Adherence to rehabilitation therapies, such as exercise, has been operationally defined as "the extent to which an individual corresponds with the quantity and quality of therapy, as prescribed by their healthcare professional" (38). The Exergames Study provided an exercise/cognitive telehealth program that incorporated aspects of known facilitators to participation in rehabilitation programs including (a) direct (virtual) supervision of sessions, (b) personalized interventions (i.e., individualized AEx and cognitive training prescriptions), and (c) sessions conducted with a 1:1–2 therapist: participant ratio to promote an environment of social support. Since the participants were delivered the needed equipment to participate in intervention sessions from their place of residence and were also able to schedule 3 sessions/week (Monday–Saturday, 7 AM to 6 PM) with the therapist, the Exergames Study was also able to combat the traditional access barriers to supervised, facility-based rehabilitation programs (39–41). Regardless, the ability of the Exergames Study to address these facilitators and barriers to therapy/rehabilitation program participation likely contributed to the high session attendance. These findings partially supported our first hypothesis that attendance would exceed 80%, as the overall attendance was 85.6% but only 78.2% (below threshold) for the Exergames group. The overall attendance was similar to another 12-week pilot telerehabilitation study conducted in persons with Parkinson's disease (22); however, direct comparisons with other telerehabilitation studies are challenging given the heterogeneity of rehabilitative programing (i.e., study length, exercise, and nonexercise training modalities) in studies focusing on neurological conditions (42–44).

Pertaining to the quality of exercise provided by the Exergames Study, moderate-intensity AEx was prescribed in the active groups based on the evidence suggesting its favorable effects on reducing AD risk and enhancing cognition (45–47). Again, participants exercised successfully at moderate intensity (13 = RPE) with 87.7% sessions achieving the RPE goal (84.3% for the Exergame group and 94.9% for the AEx group). Additionally, no significant differences were found between groups in average RPE. Overall, these findings suggest the potential of a synchronous, exercise-cognitive training telehealth program to also deliver quality AEx in persons with SCD and supported our second hypothesis. Another important finding was that the Exergame did not

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TABLE 3. Feasibility indicators of Exergame telehealth program. Data expressed as means ± SD.

Exercise Quantity/Quality Indicators	All	Exergame	AEx	Stretching	*F* Test or *t* Value	*P* Value	ES
Attendance (%)[a]	85.6 ± 18.4	78.2 ± 4.4	97.0 ± 4.4	94.0 ± 14.6	4.47	0.02	0.23
Total min exercised[a]	1,145 ± 441	1,002 ± 436	1,236 ± 449	1,341 ± 283	2.71	0.08	0.16
Average session duration (min)[a]	39.9 ± 4.7	38.7 ± 4.8	39.3 ± 5.3	41.2 ± 2.3	1.36	0.27	0.08
Average RPE[b]	12.8 ± 0.6	12.6 ± 0.6	13.0 ± 0.6	-	1.54	0.14	−0.60
% sessions RPE target was achieved[b]	87.7 ± 18.8	84.3 ± 20.9	94.9 ± 10.9	-	1.77	0.09	−0.56
Average exercise HR (relative to resting HR), (bpm)[b]	30.6 ± 12.5	29.9 ± 11.7	32.1 ± 14.5	-	0.39	0.70	−0.17

AEx = aerobic exercise only; ANOVA = analysis of variance; ES = effect size; HR = heart rate; RPE = rating of perceived exertion
[a]Comparisons made via 1-way ANOVA
[b]Comparisons made via independent samples *t* test. Effect sizes reflect η^2 (ANOVA) or Cohen's d (*t* test)

TABLE 4. Summary of AEs.

AE	Group	Type	Severity	Course of Action
Pancreatic tumor	AEx	Nonstudy related/other	Severe	Study attrition
Strained hamstring	Exergame	Nonstudy related/ musculoskeletal	Moderate	Missed final 14 sessions, participant wished to discontinue intervention but remain in study for follow-up testing.
Chest pain and dyspnea	Exergame	Study related/ cardiovascular[a]	Moderate	Referred to cardiologist. Missed 4 sessions (acid reflux) and was recleared to resume study.
Hypotensive response	Exergame	Study related/ cardiovascular[a]	Moderate	Referred to primary care provider. Missed 12 sessions and was recleared to resume study.

AE = adverse event; AEx = aerobic exercise
[a]Study-related events indicate that AE occurred during or immediately after (1 h) session. Two study-related AEs occurred in 293 training hours for the Exergame group. Collectively, there were 2 study-related AEs in 463 training hours

disrupt or prevent participants from exercising at moderate intensity (i.e., quality AEx). A worry expressed during the design of the study and intervention was that the Exergame could affect effort during cycling, as participants could potentially direct too much focus on navigating the game (and its cognitive tasks). Although it can only be speculated, perhaps the user-friendly nature of the BrainFitRx (SUS score 75.2) was a facilitator in this group maintaining moderate-intensity exercise. Of note, there was a weak to moderate correlation between exercise RPE and SUS score ($r = 0.36$; $P = 0.16$).

Safety is an important concern to exercise-focused telehealth/telerehabilitation programs, such as in the format of the synchronous, telehealth delivery model inherent to the Exergame Study. This concern is predominantly because of the limited possibility of direct intervention by the exercise therapist in the occurrence of a severe AE for which aid is required (48). Although the 2 study-related AEs occurred in the Exergame group, we can only speculate that it was by chance. However, given their nature, they likely would have occurred if the participants were randomized to the AEx group, and therefore, they are not likely attributed to the dual-task nature of exergaming. A recent systematic review was conducted to investigate the safety of exergaming in older adults (49), which indicated that there were few AEs, and the severity was described as mild and mostly attributed to discomfort (musculoskeletal pain). Of note, it should be highlighted that the authors of this systematic review revealed that most studies were conducted in a laboratory or rehabilitation setting and applied extra safety measures such as in-person supervision, walking frames, or gait belts (to reduce fall risk). Findings related to safety metrics in the Exergame Study are in line with those published in the aforementioned systematic review (49) and add to the literature, as authors of few studies have assessed the safety of the administration of exergaming in the homes of older adults. The Exergame Study promoted participant safety through the implementation of a thorough screening process for participation in the telehealth program, in the absence of a clinical stress test. Additionally, during each exercise session, vitals were

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monitored by the supervising therapist. Lastly, the seated, stationary modality of AEx cycling may have helped promote safe, moderate-intensity AEx, relative to other modes of exercise investigated in other exergaming studies (such as those involving standing on elevated platforms which are thought to present a potential risk of tripping and falling, particularly when attention is focused on the gaming display) (49).

In addition to the strengths of the intervention and thorough evaluation feasibility metrics, weaknesses must be discussed. We acknowledge that this exploratory study suffers from limitations due to the small sample size. The generalizability of the findings may be impacted by the lack of a diverse sample, as participants were 100% non-Hispanic white. Finally, the inability to gauge the effectiveness of the Exergames Study on exercise and nonexercise physical activity in the short and long term make the true assessment of sustainability impossible to fully determine.

CONCLUSIONS

Collectively, we believe that the design of the Exergames Study promoted the delivery of safe and quality AEx + cognitive training through the BrainFitRx. Our findings add to the growing evidence that exergaming is a safe and feasible model for the delivery of telehealth therapies, but in this study, we expand the clinical applicability of exergaming, as we investigated a synchronous telehealth model to deliver exergaming in persons who experience SCD, therapies that are typically conducted in in-person settings. Further controlled studies with greater sample size could help further expand the results of this study.

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