Exergaming and Older Adult Cognition

A Cluster Randomized Clinical Trial

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Background: Dementia cases may reach 100 million by 2050. Interventions are sought to curb or prevent cognitive decline. Exercise yields cognitive benefits, but few older adults exercise. Virtual reality–enhanced exercise or "exergames" may elicit greater participation.

Purpose: To test the following hypotheses: (1) stationary cycling with virtual reality tours ("cybercycle") will enhance executive function and clinical status more than traditional exercise; (2) exercise effort will explain improvement; and (3) brain-derived neurotrophic growth factor (BDNF) will increase.

Design: Multi-site cluster randomized clinical trial (RCT) of the impact of 3 months of cybercycling versus traditional exercise, on cognitive function in older adults. Data were collected in 2008–2010; analyses were conducted in 2010–2011.

Setting/participants: 102 older adults from eight retirement communities enrolled; 79 were randomized and 63 completed.

Interventions: A recumbent stationary ergometer was utilized; virtual reality tours and competitors were enabled on the cybercycle.

Main outcome measures: Executive function (Color Trails Difference, Stroop C, Digits Backwards); clinical status (mild cognitive impairment; MCI); exercise effort/fitness; and plasma BDNF.

Results: Intent-to-treat analyses, controlling for age, education, and cluster randomization, revealed a significant group X time interaction for composite executive function ($p=0.002$). Cybercycling yielded a medium effect over traditional exercise ($d=0.50$). Cybercyclists had a 23% relative risk reduction in clinical progression to MCI. Exercise effort and fitness were comparable, suggesting another underlying mechanism. A significant group X time interaction for BDNF ($p=0.05$) indicated enhanced neuroplasticity among cybercyclists.

Conclusions: Cybercycling older adults achieved better cognitive function than traditional exercisers, for the same effort, suggesting that simultaneous cognitive and physical exercise has greater potential for preventing cognitive decline.

Trial registration: This study is registered at Clinicaltrials.gov NCT01167400.

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Introduction

Dementia is a growing global epidemic with substantial personal, social, and economic costs[1] and has led to calls for interventions to prevent or slow cognitive decline.[2,3] Cross-sectional research suggests physical exercise may prevent or delay dementia,[4–6] and meta-analyses demonstrate that physical exercise improves cognitive function in normal aging[7,8] and in dementia.[9] Recent research has extended these findings to older adults with mild cognitive impairment[10–12] whose deficits are beyond those expected for their age but that

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do not interfere with daily living and yet may be a precursor to dementia.

Further, evidence is accumulating that cognitive benefits may be achieved by way of improved neuronal functions, including neurogenesis, shown by concomitant structural and functional changes in the brain,[13–17] impacts on biomarkers of Alzheimer's disease,[18,19] and increases in brain-derived neurotrophic growth factor (BDNF).[10,14,19,20] Cognitive benefit from exercise is found primarily in executive control and frontal lobe functions, such as planning, divided attention, and inhibition of responses.[8,21,22] These abilities are often impaired in dementia and are key to maintaining independence and delaying institutionalization.

The demonstrated cognitive and health benefits of exercise are such that the American College of Sports Medicine (ACSM) and the American Heart Association (AHA) upgraded recommended daily exercise.[23] Yet data from the CDC Healthy People 2010 Database indicate that only 14% of adults aged 65–74 years and 7% of those aged >75 years reported regular exercise. Physician prescription of exercise[24] has not been shown to substantially increase participation; <4% of patients in one study complied.[25] These data suggest the need for more-compelling interventions to increase the motivation of older adults to exercise, as well as multimodal interventions that address the multiple deficits from physical inactivity.[26]

Virtual reality–enhanced exercise or "exergames" combine physical exercise with computer-simulated environments and interactive videogame features and have become popular as a means to promote healthy behaviors[27] and increase the appeal of exercise (e.g., the Wii Fit and PlayStation Move).[28] Exergames have the potential to increase exercise by shifting attention away from aversive aspects and toward motivating features such as competition and three-dimensional (3D) scenery. Participation in exergaming compared with traditional exercise can lead to greater frequency and intensity[29] and enhanced health outcomes.[28,30,31] A recent study[32] reported that compared with traditional stationary cycling, older adults preferred cycling with interactive gaming.

Although promising, there are limited published data on whether interactive exergaming technologies are reliably associated with enhanced physical and cognitive health outcomes, and more-controlled research on the effects of health games is needed.[27,33] One early study[34] investigated virtual reality–enhanced stationary cycling using virtual tours and on-screen competition (referred to here as "cybercycling") and found cognitive improvement in patients with traumatic brain injury. However, without a traditional exercise control group, it is unclear whether cybercycling yielded cognitive benefit beyond physical exercise alone.

While there are reports of the psychological benefits of cybercycling,[29,30,35] no previous randomized clinical trial (RCT) has evaluated the cognitive benefits of virtual reality–enhanced exercise. Presented herein are results of the Cybercycle Study, a multi-site cluster RCT in which the cognitive benefit of cybercycling was compared with traditional stationary cycling, for older adults living independently. On the basis of prior research[8,21,22] showing primarily executive function gains from exercise, it was hypothesized that cybercycling would yield greater executive function. Further, it was hypothesized that any change would be due to increased exercise effort spurred on by engaging interactive virtual tours, competition, and added mental challenge. Secondary analyses examined change in BDNF as a biomarker indicating possible neuroplasticity, which has been implicated as a mechanism of change linking exercise to cognition.[10,14,18–20]

Methods

Design

This cluster RCT (2008–2010) compared the impact on executive function of two exercise interventions: physical exercise alone and physical plus mental challenge as combined in an exergame.

Setting and Participants

Participants were recruited by fliers and information sessions at eight independent living facilities. The facilities were chosen because of proximity to investigator institutions; similarity in size (average 100–200 residents); and presence of contiguous living areas to ensure indoor access to a study bike (to minimize barriers associated with travel). Participants volunteered based on demonstrations of cybercycle functionality, not knowing which condition they would be randomized to, but aware that all could use the cybercycle after the 3-month intervention. Volunteers aged ≥55 years were screened; exclusion criteria were known neurologic disorders (e.g., Alzheimer's or Parkinson's) and functional disabilities that would substantially restrict participation in cognitive testing or exercise. Written physician approval was required.

Union and Skidmore Colleges' IRBs approved the study; participants provided written informed consent. A priori sample size estimates were calculated based on published effect sizes for cognitive ($d=0.48$)[8] and physiologic ($d=0.41$)[36] outcomes from physical exercise. An a priori power analysis had found that in a 2 × 2 (group × time) design, a sample of 100 would achieve 0.82 power to detect a significant effect ($p=0.05$). However, for logistic reasons, the study design was changed from individual to cluster randomization. Post hoc statistical power is reported in the Results section.

Interventions

Participants in the cybercycle and control conditions rode identical recumbent stationary bikes, except for the virtual reality display that was enabled on the cybercycle (Appendixes A and B, available online at www.ajpmonline.org). Participants were trained in the use of the bike, log-in procedures, and paper log for recording ride statistics as a backup to the computer. Participants were given a target heart rate range to maintain during exercise using the Heart Rate Reserve (HRR) method[23]; mid-intervention adjustments were made to maintain a relative HRR of 60%.

A 1-month familiarization period allowed participants to learn to attend to continuous biofeedback information for safety (e.g., heart rate), before introducing distracting virtual tours in the cybercycle condition. Participants were instructed to gradually increase exercise frequency to 45 minutes per session five times per week consistent with the ACSM and AHA recommendations.[23] Individual progress reports and leaderboards were posted weekly to control goal-setting and competition across interventions. Participants were asked to hold constant other lifestyle factors (e.g., diet and other physical activity) during their study participation to isolate the effect of the interventions. The minimum threshold for "completers" was 25 rides during the intervention period; thus "completers" rode an average of three rides per week minus 2 weeks' allowance for illness, holidays, or equipment repair.

Cybercycle group. After 1 month of familiarization, cybercycle participants experienced 3D tours and competed with their own "ghost" rider (last best ride). During Month 3, participants were instructed to outpace on-screen riders.

Control group. After 1 month of familiarization, controls continued to ride the traditional stationary bike viewing biofeedback information (e.g., heart rate and mileage). Each month, placebo training (e.g., hydration and stretching) matched the attention given to the cybercycle group.

Randomization. A priori plans were for individual random assignment through software controls, but equipment problems, combined with limited funding and space, led to cluster assignment in order to limit cross-condition contamination. Sites were selected by random draw. Cluster random assignment achieved similar levels of cognitive function and physiologic status at pretest, although the groups differed in age and education, which were entered as covariates in analyses ($p=0.002$ and $p<0.001$, respectively; Table 1).

Main Outcome Measures

Cognitive assessment. Cognitive testing was done at enrollment (baseline), 1 month later (pre-intervention), and 3 months later (post-intervention). Analyses were conducted using pre- and post-scores. Baseline testing minimized the impact of practice and learning effects associated with serial assessments and provided a more stringent test of the main hypothesis.[37] Blinded ratings were achieved in most cases. The primary cognitive outcome of interest, executive function, was assessed via Color Trails 2-1 difference score (time to connect alternating color and number dots, minus time to connect only numbered dots)[38]; Stroop C (time to name color of ink of contrasting color word)[39]; and Digit Span Backwards (number of correct trials repeating a string of numbers in reverse order).[40]

To reduce the number of statistical comparisons, an executive function composite score was obtained by converting raw scores on each test to *z*-scores using the grand mean and SD across both groups for each time point, then averaging the three measures (Cronbach's $\alpha=0.67$). Timed tasks were reversed; a positive value on the composite indicates a score above the mean. Secondary

Table 1. Baseline characteristics of trial participants, M (SD) unless otherwise indicated

	Cybercycle ($n=38$)	Control bike ($n=41$)
Age (years)[a]	75.7 (9.9)	81.6 (6.2)
Women (n [%])	33 (70.7)	29 (86.8)
Education (years)[a]	12.6 (2.2)	14.8 (2.3)
Physiologic factors		
Weight (kg)	75.0 (13.1)	72.1 (15.9)
BMI	29.0 (4.7)	27.4 (6.3)
Fat mass (kg)	31.8 (8.0)	28.0 (11.7)
Lean mass (kg)	40.6 (6.3)	41.9 (6.8)
Abdominal fat (%)	47.4 (8.4)	39.9 (12.4)
Insulin (uU/mL)	10.7 (5.0)	9.9 (8.0)
Glucose (mM/L)	6.4 (2.0)	5.5 (0.6)
Physical activity level (daily kcal)[b]	301.3 (218.0)	307.2 (215.3)
NEUROPSYCHOLOGIC MEASURES		
Intelligence proxy (NAART), IQ	117.6 (8.7)	120.6 (5.2)
Executive function		
Color Trails Difference (2-1; s)	55.2 (30.7)	75.6 (64.8)
Stroop C (s)	67.3 (35.7)	68.7 (35.8)
Digits Backwards (sum score)	5.8 (1.9)	6.5 (2.1)
Attention		
LDST (sum score)	29.2 (7.1)	29.1 (6.6)
Verbal fluency		
COWAT (sum score)	33.1 (15.5)	37.8 (12.4)
Categories (sum score)	15.9 (4.2)	16.1 (4.6)
Verbal memory (immediate)		
RAVLT (sum 5 trials score)	36.1 (12.1)	38.9 (9.5)
RAVLT immediate recall (score)	7.2 (2.9)	7.2 (3.8)
Verbal memory (delayed)		
RAVLT delayed recall (score)	6.9 (3.6)	6.8 (3.9)
Fuld delayed recall (score)	7.6 (2.7)	7.2 (1.8)
Visuospatial skill		
Figure copy (sum score)	26.3 (5.8)	27.1 (7.2)
Clock (sum score)	5.8 (1.4)	6.1 (1.3)

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Table 1. Baseline characteristics of trial participants, M (SD) unless otherwise indicated *(continued)*

	Cybercycle (n=38)	Control bike (n=41)
Visuospatial memory (delayed)		
Figure delayed recall (score)	8.8 (6.2)	9.6 (4.7)
Motor function		
Pegboard dominant hand (s)	120.7 (50.1)	130.0 (44.6)
Pegboard nondominant hand (s)	136.1 (85.7)	139.3 (47.1)
Clinical status (n [%])		
MCI (≥1 domain: ≤ −1.5 SD of norm)	16 (42.1)	14 (34.1)

[a] Group difference at baseline on age (p=0.002) and education (p<0.001)

[b] Physical activity level (daily kilocalories) was estimated in Year 1 via questionnaire and Year 2 via Actical (see Methods)

COWAT, Controlled Oral Word Association Test; IQ, intelligence quotient; LDST, Letter Digit Symbol Test; MCI, mild cognitive impairment; NAART, North American Adult Reading Test; RAVLT, Rey Auditory Verbal Learning Test

cognitive outcomes were included to characterize the sample (e.g., clinical status below); no changes were expected on these tests (Appendix C, available online at www.ajpmonline.org). At the completion of the study, participants' clinical status pre- and post-intervention was classified according to "typical" diagnostic criteria[41,42] for mild cognitive impairment (MCI; performance ≤1.5 SD on at least one subtest in the domains of executive function, verbal fluency, verbal memory, visuospatial skill, and visuospatial memory compared to normative data).[40] MCI incidence was comparable to prior research (Table 1).[43]

Physiologic Assessment

Baseline and post-exercise measurements included: weight (kilograms); height (centimeters); BMI; total and abdominal body composition (fat and lean mass) using the iDXA (GE Lunar, Inc.); muscle strength of quadriceps and hamstrings using the HUMAC Cybex Dynamometer (CSMI Solutions, Inc.); and insulin and glucose (Millipore, Inc.).

Assessment of Exercise Behavior

During the first year, daily physical activity (kilocalories) was measured using the Aerobics Center Longitudinal Study Physical Activity Questionnaire (ACLS-PAQ).[44] METs were used to compute energy expended in activities. In the second year, additional resources allowed measurement of daily physical activity (kilocalories) using an accelerometer (Actical; Phillips Respironics, Inc). Ride behaviors (frequency, intensity, and duration) were recorded on the bike computer and by participants in a paper log.

Neuroplasticity Assessment

Fasting morning plasma samples were collected during pre- and post-evaluations, not after exercise. Brain-derived neurotrophic factor (BDNF) levels were analyzed via enzyme-linked immunosorbent assay (ELISA; Chemicon, Millipore, Billerica, MA; see Appendix D, available online at www.ajpmonline.org).

Statistical Analysis

Data were analyzed using SPSS, version 19.0. For normally distributed continuous variables, arithmetic Ms and SDs were calculated. For comparisons between groups of categoric baseline data, chi-square analyses were conducted. For comparisons of continuously distributed baseline and demographic variables, t tests were performed. Intent-to-treat analysis was conducted using the last observation carried forward (LOCF). Four analytic strategies were employed to examine between-group changes in outcomes: intent to treat, complete case, age matched, and comparison of completers and noncompleters.

Mixed linear modeling, including fixed and random effects, estimated the impact of the interventions on executive function composite scores, when adjusted for age, education, and nested variability in clusters (eight sites). A likelihood ratio test was conducted to compare the full and restricted models, with and without sites nested. Follow-up repeated measures general linear models (GLMs) examined the group X time interaction effect, first by examining the multivariate omnibus test (to control Type I error), then examining the univariate results for the three executive function measures. To test whether between-group differences in cognitive outcomes were due to differential exercise effort, t-tests were used. Effect sizes were computed using Cohen's d formula with pooled SDs. Tests of significance used a two-sided alpha of p=0.05.

Results

A CONSORT flow chart (Figure 1) shows that 102 independent-living, older adults from eight retirement communities met criteria and consented to participate; 79 began exercise training and were randomized by site (average cluster n=10, SD=3.6; Figure 1). Sixty-three older adults, ranging in age from 58 to 99 years, completed the study (80% of randomized).

Effect of the Intervention on Cognitive Function, Physical Health, and Exercise Behaviors

The group X time interaction effects for executive function of the full and restricted mixed linear models were highly similar (F[1, 51.8]=10.4, p=0.002; F[1, 76.2]=10.4, p=0.002, with and without sites nested, respectively; Figure 2). There was no benefit of adding the cluster random effect (LR $\chi^2[1]=3.16$, p=0.93); thus, in order to maximize df in this relatively small sample, the least-restrictive fitting model was selected and subsequent parsimonious analyses were chosen. A difference between groups in change in executive function over 3 months was indicated by a group X time interaction in a

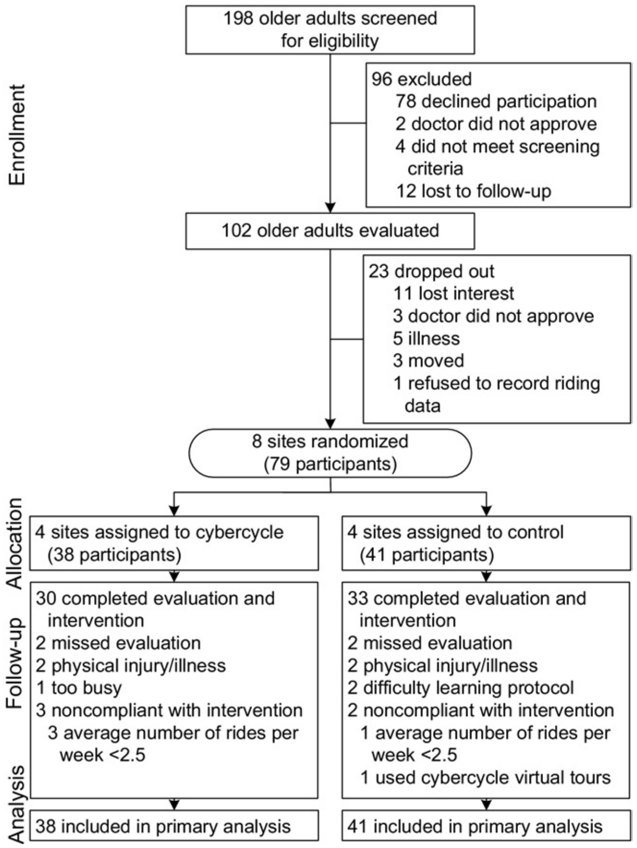

Figure 1. CONSORT diagram showing flow of participants from screening to post-exercise evaluation

multivariate repeated measures GLM of Color Trails Difference, Stroop C, and Digits Backwards, simultaneously and revealing a large effect (F[3, 62]=5.50, $p=0.002$, $\eta_p^2=0.21$, power=0.93). Given the significant omnibus test, univariate group X time interactions were examined and found significant for all three measures of executive function (Table 2).

Planned simple effects analyses controlled for age, education, and cognitive performance at baseline and revealed an increase in performance on the Color Trails Difference ($p=0.01$) and Stroop C ($p=0.05$) tests for cybercyclists, with no change for controls. Cybercyclists maintained a steady performance on Digits Backward, whereas the control group declined ($p=0.01$). No interaction effects were found on physiologic or secondary cognitive outcomes (Table 2). Analyses were repeated using age-matched and complete-case subsamples and results were similar (Appendixes E–H, available online at www.ajpmonline.org). No differences in exercise frequency, intensity, or duration were found between the cybercyclists and controls (Table 3). While the average energy expended was relatively low (approximately 100 calories/ride), research has shown that even low-intensity exercise (100 calories) can serve as an adequate training stimulus among sedentary older adults.[45]

Cybercycling yielded a medium average effect size for executive function that was over and above the average effect for traditional exercise ($d=0.50$), contrasted with prior research that showed a small effect size for aerobic exercise over and above nonaerobically exercising controls ($d=[0.48-0.16]=0.32$).[51] Cybercyclists experienced a 23% reduction in risk of clinical progression to MCI compared with traditional exercisers (nine controls versus three cybercyclists converted to MCI). That is, using the "typical" diagnostic criteria for MCI,[41,42] these participants began the trial with performances in the normal range, but experienced a decline to −1.5 SD below normative data on at least one test within those domains.

Adherence to prescribed exercise (79.7%) was comparable with prior research (78.2%).[12] Consistent with CONSORT standards, a comparison of study completers and noncompleters is reported. Similar rates on noncompletion were found in both conditions; at baseline, noncompleters were more compromised than completers on some cognitive and physiologic measures that may have led to greater difficulty completing the study (Appendix G, available online at www.ajpmonline.org). Appendix I (available online at www.ajpmonline.org) shows the 13 adverse events in the study.

Biomarker Evidence of Possible Neuroplasticity: Brain-Derived Neurotrophic Growth Factor Results

Plasma BDNF data from 30 participants were available (ages 66–89 years). A significant group (cycle condition)

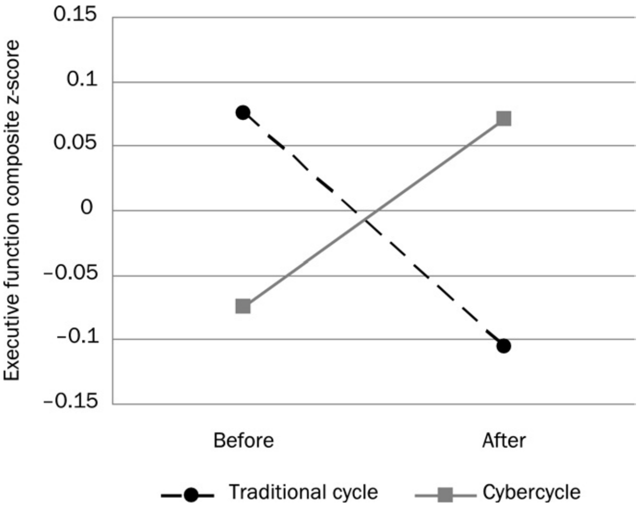

Figure 2. Change in executive function composite before and after 3 months of exercise

Note: $n=79$; mixed linear model (random effects: age, education, and cluster) group X time interaction is significant ($p=0.002$).

Table 2. Neuropsychologic and physiologic outcomes after 3 months of exercise (intent-to-treat analysis)[a]

	Mean difference from baseline (95% CI)		
	Cybercycle (n=38)	Control bike (n=41)	p-value (df)[b]
PRIMARY COGNITIVE OUTCOMES			
Executive function			
Color trails difference (2-1) (s)	−15.94 (−16.21, 15.66)	9.74 (9.48, 10.00)	0.007 (1, 73)
Stroop C (s)	−6.59 (−6.67, −6.51)	0.56 (0.49, 0.64)	0.05 (1, 73)
Digits backwards (sum score)	0.36 (0.34, 0.38)	−0.83 (−0.85, −0.82)	0.03 (1, 73)
SECONDARY COGNITIVE OUTCOMES[c]			
Attention			
LDST (sum score)	0.79 (0.62, 0.95)	0.73 (0.57, 0.89)	0.95 (1, 72)
Verbal fluency			
COWAT (sum score)	3.51 (2.77, 4.25)	2.33 (1.62, 3.03)	0.63 (1, 73)
Categories (sum score)	−0.03 (0.11, −0.18)	1.18 (1.32, 1.04)	0.22 (1, 73)
Verbal memory (immediate)			
RAVLT (sum 5 trials score)	−0.73 (−1.27, −0.19)	0.85 (0.33, 1.37)	0.50 (1, 73)
RAVLT immediate recall (score)	0.77 (0.60, 0.94)	0.06 (−0.10, 0.22)	0.32 (1, 73)
Verbal memory (delayed)			
RAVLT delayed recall (score)	0.71 (0.62, 0.79)	0.10 (0.01, 0.18)	0.43 (1, 73)
Fuld delayed recall (score)	0.15 (0.13, 0.17)	0.39 (0.37, 0.41)	0.61 (1, 73)
Visuospatial skill			
Figure copy (sum score)	3.27 (3.56, 2.98)	3.69 (3.97, 3.40)	0.81 (1, 72)
Clock (sum score)	0.07 (0.07, 0.07)	−0.19 (−0.19, −0.19)	0.45 (1, 72)
Visuospatial memory (delayed)			
Figure delayed recall (score)	0.07 (0.22, −0.08)	1.66 (1.80, 1.52)	0.28 (1, 72)
Motor function			
Pegboard dominant hand (s)	10.61 (8.64, 12.57)	6.13 (4.22, 8.03)	0.56 (1, 72)
Pegboard nondominant hand (s)	7.76 (5.86, 9.65)	13.79 (11.95, 15.63)	0.36 (1, 72)
PHYSIOLOGIC OUTCOMES			
Weight (kg)	−0.63 (−0.75, −0.52)	−0.04 (−0.15, 0.07)	0.24 (1, 72)
BMI	−0.26 (−0.29, −0.23)	−0.03 (−0.06, 0.00)	0.26 (1, 67)
Fat mass (kg)	−1.04 (−0.95, −1.13)	−0.76 (−0.67, −0.84)	0.50 (1, 72)
Lean mass (kg)	0.39 (0.31, 0.47)	0.56 (0.48, 0.63)	0.65 (1, 72)
Abdominal fat (%)	−1.79 (−1.97, −1.61)	−0.94 (−1.11, −0.78)	0.32 (1, 66)
Leg extension 60° (s^{-1})	−2.96 (−3.00, −2.92)	11.09 (11.05, 11.13)	0.04 (1, 71)
Leg flex 60° (s^{-1})	−2.79 (−3.26, −2.31)	5.70 (5.25, 6.15)	0.07 (1, 71)
Insulin (uU/mL)	2.75 (2.39, 3.12)	1.53 (1.16, 1.90)	0.46 (1, 67)
Glucose (mM/L)	−0.09 (−0.01, −0.16)	−0.06 (0.01, −0.13)	0.90 (1, 68)

[a] Marginal mean differences and CIs reported, based on repeated measures ANCOVA controlling for age and education

[b] For ANCOVA, repeated measures, group X time; the first df in parentheses refers to the effect (group X time) and the second refers to the error term

[c] No significant changes expected given prior research literature

COWAT, Controlled Oral Word Association Test; LDST, Letter Digit Symbol Test; RAVLT, Rey Auditory Verbal Learning Test

Table 3. Exercise behavior outcomes after 3 months of exercise: cybercycle vs control bike[a]

	M (SD)			
Exercise behavior outcomes	**Cybercycle (n=30)**	**Control bike (n=33)**	**Difference between interventions (M [95% CI])**	***p*-value (df)**
Frequency of rides (n)	51.3 (3.32)	53.3 (3.14)	−1.96 (−2.31, −1.61)	0.68 (1, 59)
Power (watts)[b]	36.3 (3.28)	32.1 (3.15)	4.20 (3.93, 4.46)	0.44 (1, 31)
Energy expended (kcal)	107.9 (8.05)	93.6 (7.63)	14.32 (13.47, 15.17)	0.23 (1, 59)
Duration (min)	35.5 (1.81)	33.8 (1.72)	1.61 (1.42, 1.80)	0.54 (1, 59)
Distance average (miles)	5.4 (0.40)	4.8 (0.38)	0.65 (0.61, 0.69)	0.27 (1, 59)
Distance total (miles)	283.9 (28.80)	261.4 (27.29)	22.51 (19.47, 25.54)	0.59 (1, 59)
Speed average (mph)[b]	7.4 (0.38)	8.3 (0.37)	−0.83 (−0.86, −0.80)	0.19 (1, 31)
Speed peak (mph)[b]	10.7 (0.39)	9.8 (0.37)	0.97 (0.94, 1.00)	0.13 (1, 31)
Physical activity daily (kcal)	324.4 (32.91)	304.2 (32.22)	20.22 (0.94, 1.00)	0.66 (1, 43)

[a] Marginal Ms and SDs reported, based on ANCOVA controlling for age and education
[b] Sample sizes: cybercycle (n=17) and control bike (n=18) because of enhanced ride data available in Year 2
mph, miles per hour

X time (pre- and post-intervention) interaction, with age and education as covariates, was found, revealing that cybercyclists experienced a greater increase in BDNF than traditional exercise (Appendix J, available online at www.ajpmonline.org; $F[1, 25]=4.89$; $p=0.05$).

Discussion

This cluster RCT provides preliminary evidence that exergaming can yield greater cognitive benefit, buffering against decline, more so than traditional exercise alone. Older adults in an independent-living facility who exercised on a virtual reality–enhanced cybercycle for 3 months had significantly better executive function than those expending similar effort on a traditional stationary bike. In contrast with prior research showing a small effect of exercise over and above controls,[8] cybercycling produced a medium effect that was over and above traditional exercise, with average improvements in performance of one half SD. Additionally, fewer cybercyclists converted to MCI, suggesting a reduction in risk of progression to MCI; however, the incidence and rate of conversion to MCI herein might be higher than in a community-dwelling sample, and further research is needed to establish replicability and generalizability.

Contrary to expectations, effort and fitness did not appear to be the factors behind differential cognitive benefits found in the cybercycle group. Perhaps because this was a prescriptive intervention, most participants across both groups were compliant with the regimen, and further research is needed to evaluate whether naturalistic use would lead to greater effort by cybercyclists. These findings are consistent with some assertions in the literature that the cognitive benefit derived from exercise is not necessarily tied to fitness outcomes, although the debate continues.[46,47]

Future research will be needed to tease apart the contributions of a variety of factors in the cybercycling condition. Consistency across conditions for goal setting and competition suggests virtual reality imagery and interactive decision making might be the potent factors of the cybercycle. Exit interviews provided anecdotal evidence of the value of these unique features. Participants commented on their enjoyment of visual stimulation and the challenge of outpacing avatars. One woman, aged 86 years, noted that she felt healthier and attributed this to actively maneuvering to "compete with that fellow ahead of me!" Cybercycling provides a different experience than other cognitive stimulation such as TV, because it is interactive.

One explanation for the greater cognitive benefit found with cybercycling compared with traditional cycling could be that the effect is due directly to the added mental exercise required. Given that both exercise intervention samples exerted similar effort over 3 months, the main difference between the two interventions was the virtual reality experience. Navigating a 3D landscape, anticipating turns and competing with others, requires additional focus, expanded divided attention, and enhanced decision making. These are activities that depend in part on executive function, which was significantly affected. A direct impact of cognitive stimulation herein does resonate with a growing, but formative literature on the effects of cognitive training.[48] While research is mixed and transfer is debatable, some research supports the utility of mental exercise to facilitate cognitive health in older adults.[49–52] Future research should measure the amount of cognitive stimulation participants engage in during the period of an exercise intervention to clarify the potential added benefit of activities beyond physical exercise.

Another explanation for the greater cognitive benefit found for cybercycling could be that the effect is due to the interactive nature of combined physical and cognitive exercise. Perhaps cybercyclists benefit from a dual-exercise experience, accruing the positive effects of intertwined cognitive and physical exercise. When comparing average effect sizes in the literature,[51] controls demonstrate test–retest growth (0.16), cognitive stimulation alone yields a comparable negligible effect (0.13), physical exercise yields a small effect over and above controls (0.32), while combined cognitive and physical exercise herein produced a medium effect beyond that traditionally found for exercising controls (0.50). It is interesting that the combined effect of cognitive and physical exercise exceeds the sum of effects noted in the literature above, perhaps indicating a compounding or synergistic effect of cybercycling. Future research could evaluate this by comparing cognitive stimulation alone, physical exercise alone, and the combination of the two.

Compounding cognitive benefit from a combined task does fit with the evolving understanding of the mechanisms of brain plasticity and the role of exercise and enriched environments in inducing angiogenesis, neurogenesis, and other changes that foster neurovascular integrity.[15,53] A combined effect would be consistent with the animal literature, where cognitive benefit from physical exercise and mental stimulation has been found to occur by different mechanisms (cell proliferation and cell survival, respectively).[53–55] This combined-effect hypothesis expands on prior research in humans, which has found enhanced cognitive benefits of physical and cognitive exercise interventions administered in tandem.[56,57] Similarly, these findings fit with prior research that indicates cognitive benefit beyond that from traditional exercise, when physical exercise is cognitively challenging (e.g., Tai Chi or dancing).[58–60]

To further illuminate possible mechanisms linking exercise to cognitive change, alternative measures of intermediary physiologic or brain "fitness" (e.g., neurotrophic growth factors), may be needed beyond cardiovascular fitness outcomes typically assessed.[61] In this study, it was found that cybercyclists experienced a significantly greater increase in BDNF than traditional exercisers, suggesting that exercise may lead to cognitive benefits by way of biomarkers linked to neurotrophic effects. The literature on BDNF change with physical exercise is mixed, and researchers continue to evaluate possible moderators such as age, gender, and type of exercise.[10,14,20] Cybercyclists exhibited a significant change in BDNF, which does fit with research that has shown a significant increase in BDNF after computerized cognitive training.[62]

Compared with prior research on the effects of physical exercise alone, the effect of the cybercycle intervention adds to the growing consensus that exercise has a consistent effect on executive functions.[8,21,22] However, the control group herein was also an exercising group (consistent with recommendations),[63] but did not show pre- to post-test improvement on executive function. It appears the added rigor of using an additional pre-test for familiarization did "wash-out" practice advantages[37] evident in prior studies. While traditional exercise did not yield "improvement" in cognition, it may have slowed decline, which would be consistent with some prior research which found that in a similarly aged sample, the control group declined on cognitive function.[64]

Limitations of this study include unequal representation of age and education in the groups despite randomization, and while statistical controls were used and age- and education-matched post hoc analyses were conducted, future research could prospectively match on these variables. Also, participants had a relatively high level of education, and ethnic variability was limited; additional research is needed to test generalizability. Noncompleters performed worse on some cognitive and physiologic measures; thus, screening for minimum levels of function may be advisable.

Several strengths of this study are noteworthy. This study addresses a gap in the literature as no prior RCT has compared cognitive benefits for older adults of virtual reality–enhanced exercise with traditional exercise. The observed effect exceeds that typically reported in traditional exercise research. The intervention should be applicable to a wide range of older adults in an independent living context given the ease of using a recumbent bike and increasing availability of exergaming technologies. The finding that cognitive outcomes could be improved with cybercycling over and above those from traditional exercising is surprising in light of similar exercise effort, but this also provides an intriguing issue to explore in future research.

Follow-up studies could aim to replicate prior research by using neuroimaging to examine the impact of exergaming on the brain for further evidence of neuroplasticity.[13–16] With a refined experimental design, future research could clarify if cognitive exercise alone is sufficient to produce the observed cognitive change, or if exergaming leads to added benefit by synergistic neurophysiologic advantages when mental challenges are linked to physiologic movements. Future research could compare outdoor street-cycling with cybercycling, since the natural world, street obstacles, other cyclists, and way-finding would similarly create cognitive challenge. It would also be interesting to evaluate biophilia factors, degree of cognitive stimulation, and social presence. Additionally, some labs have full-surround audio-visual virtual reality environments, that could allow controlled testing of "outdoor" factors while ensuring safety.[65] Last, a cost–benefit analysis would be useful, in light of reports that physical activity interventions for inactive older adults can be cost effective.[66]

In summary, this cluster RCT indicates that for older adults, virtual reality–enhanced interactive exercise or "cybercycling" two to three times per week for 3 months yielded greater cognitive benefit and possibly added protection from progression to MCI, compared with a similar dose of traditional exercise. Additional research is needed to examine the cause of this curious finding, which may be due to the presence of unique mental stimulation in virtual reality, or the interactive combination of cognitive and physical challenges wielding dual impacts, perhaps promoting neuroplasticity via multiple pathways.[53,54] The implication is that older adults who choose exergaming with interactive physical and cognitive exercise, over traditional exercise, may garner added cognitive benefit and perhaps prevent decline, all for the same exercise effort.

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Appendix

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.amepre.2011.10.016.

A pubcast created by the authors of this paper can be viewed at http://www.ajpmonline.org/content/video_pubcasts_collection.