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Resistance Training Promotes Cognitive and Functional Brain Plasticity in Seniors With Probable Mild Cognitive Impairment

Cognitive decline is a pressing health care issue. Worldwide, 1 new case of dementia is detected every 7 seconds.[1] Mild cognitive impairment—a well-recognized risk factor for dementia[2]—represents a critical window of opportunity for intervening and altering the trajectory of cognitive decline in seniors.

Exercise is a promising strategy for combating cognitive decline. Both aerobic training (AT) and resistance training (RT) enhance cognitive performance and functional plasticity in healthy, community-dwelling seniors[3-5] and those with mild cognitive impairment.[6] However, to our knowledge, no intervention study has compared the efficacy of both types of exercise on cognitive function and functional brain plasticity in seniors with mild cognitive impairment. Understanding this is crucial to using exercise as a strategy for altering the trajectory of cognitive decline in seniors with mild cognitive impairment.

We conducted a proof-of-concept, single-blinded, randomized controlled trial primarily designed to provide preliminary evidence of efficacy of both RT and AT to improve executive cognitive functions—robust predictors of conversion from mild cognitive impairment to Alzheimer disease[7]—in senior women with probable mild cognitive impairment. Secondarily, we aimed to examine the effect of both types of exercise on associative memory performance, everyday problem solving ability, regional patterns of functional brain plasticity, and physical function.

Methods. The EXCEL (EXercise for Cognition and Everyday Living) study was a 6-month randomized trial. Eighty-six community-dwelling women 70 to 80 years old were randomly allocated to twice-weekly RT (28 women), twice-weekly AT (30 women), or twice-weekly balance and tone (BAT) training (control group) (28 women). Participants were classified as having probable mild cognitive impairment if they had a score lower than 26 out of 30 on the Montreal Cognitive Assessment[8] and had subjective memory complaints.

The primary outcome measure was Stroop Test[9] performance, an executive cognitive test of selective attention/conflict resolution. Secondary measures of executive cognitive functions included set shifting (Trail Making Tests) and working memory (Verbal Digits Tests). Broader effects of exercise training on cognitive function were examined by assessing associative memory (memorizing face-scene pairs) and everyday problem solving ability (Everyday Problems Test). Regional patterns of functional brain plasticity were assessed using functional magnetic resonance imaging (fMRI) during the associative memory task. Finally, we assessed general balance and mobility (Short Physical Performance Battery) and general cardiovascular capacity (Six-Minute Walk Test).

The 60-minute classes were led by certified fitness instructors. For RT, both a Keiser Pressurized Air system and free weights were used.[3] Participants performed 2 sets of 6 to 8 repetitions, and loading was increased when sets were completed with proper form. The AT program was an outdoor walking program. The training stimulus started at 40% of a participant's age-specific target heart rate (ie, heart rate reserve [HRR]) and progressed to 70% to 80% of the HRR. The BAT program consisted of stretching, range of motion, balance exercises, and relaxation techniques.[3] This group served to control for confounding variables. Participants were questioned about the presence of any adverse effects and were monitored by instructors.

Results. Of the 86 participants, 77 completed the 26-week trial (26 in the RT group, 24 in the AT group, 27 in the BAT group). Twenty-two participants were included in our fMRI analysis (7 in the RT group, 7 in the AT group, and 8 in the BAT group).

The **Table** shows the baseline characteristics of our sample and change in scores from baseline to trial completion for the primary and secondary outcome measures, excluding fMRI. Compared with the BAT group, the RT group significantly improved performance on the Stroop Test ($P=.04$) and the associative memory task ($P=.03$). Compared with the BAT group, RT also led to functional changes in 3 regions of the cortex—the right lingual ($P=.03$) and occipital-fusiform ($P=.02$) gyri and the right frontal pole ($P=.03$)—during the encoding and recall of associations. In addition, there was a significant positive correlation between change in hemodynamic activity in the right lingual gyrus and change in behav-

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Table. Baseline Characteristics of Trial Participants and Mean (SD) Change in Outcome Measures at Trial Completion From Baseline in 86 Women

Variable	Mean (SD)			
	BAT Group (n = 28)	AT Group (n = 30)	RT Group (n = 28)	Total (n = 86)
Age, y	75.1 (3.6)	75.6 (3.6)	73.9 (3.4)	74.9 (3.5)
Height, cm	158.2 (7.3)	159.2 (5.9)	158.7 (7.0)	158.7 (6.7)
Weight, kg	66.4 (14.0)	64.8 (12.8)	65.2 (10.7)	65.4 (12.4)
Physical activity scale for the elderly	133.2 (78.1)	121.6 (52.9)	151.8 (74.9)	135.2 (69.52)
Education, count (%)				
<Grade 9	0	2 (2.3)	0	2 (2.3)
Grades 9-12 without certificate or diploma	5 (5.8)	3 (3.5)	2 (2.3)	10 (11.6)
High school certificate or diploma	7 (8.1)	7 (8.1)	7 (8.1)	21 (24.4)
Trades or professional certificate or diploma	5 (5.8)	2 (2.3)	3 (3.5)	10 (11.6)
University certificate or diploma	8 (9.3)	8 (9.3)	8 (9.3)	24 (27.9)
University degree	3 (3.5)	8 (9.3)	8 (9.3)	19 (22.1)
Geriatric depression scale[a]	1.0 (1.8)	1.1 (1.8)	1.4 (2.0)	1.2 (1.8)
Functional comorbidities index[b]	2.6 (2.2)	2.9 (1.5)	3.0 (1.9)	2.8 (1.8)
Instrumental activities of daily living[c]	7.8 (0.5)	7.8 (0.5)	7.7 (0.8)	7.8 (0.6)
Montreal Cognitive Assessment[d]	22.5 (2.8)	22.2 (2.8)	21.4 (3.4)	22.1 (3.0)
Mini-Mental State Examination[d]	27.1 (1.7)	27.4 (1.5)	26.0 (5.6)	26.8 (3.5)
Exercise class compliance,[e] %	59 (14.8)	60 (18.7)	54 (14.7)	57 (16.1)
Mean change in outcome measures[f]				
Stroop CW – Stroop C, seconds	1.37 (15.26)	8.83 (41.86)	9.13 (19.88)	NA
Trail Making Test B – Trail Making Test A,[g] seconds	–0.39 (40.27)	18.28 (72.55)	–0.91 (43.91)	NA
Digit forward – digit backward[h]	2.00 (3.14)	0.54 (4.77)	0.73 (2.52)	NA
Item memory	0.21 (0.76)	0.55 (1.25)	0.38 (0.75)	NA
Associative memory	0.23 (0.66)	–0.09 (0.82)	0.61 (0.72)	NA
Everyday Problem Solving Test[i]	–1.89 (4.51)	–0.91 (4.46)	–1.40 (5.39)	NA
Short Physical Performance Battery score[j]	0.70 (1.77)	1.37 (1.34)	0.40 (1.41)	NA
Six-Minute Walk Test,[k] m	4.50 (34.52)	18.73 (54.63)	11.85 (41.09)	NA

Abbreviations: AT, aerobic training; BAT, balance and tone; C, Stroop test colored X's condition (control condition); CW, Stroop test color words condition; NA, not applicable; RT, resistance training.

[a] Maximum was 15 points.

[b] Maximum was 18 points.

[c] Maximum was 8 points.

[d] Maximum was 30 points.

[e] Calculated as (total number of classes attended out of 50 classes) × 100.

[f] Measure of set shifting.

[g] Mean change for all cognitive measures (except for Associative Memory and Everyday Problem Solving Test) = baseline value minus final value. Positive change indicates improvement. Mean change for all performance measures, Associative Memory, and Everyday Problem Solving Test = final value minus baseline value. Positive change indicates improvement. Unless otherwise indicated, data are expressed as means (SDs). Percentages have been rounded and may not total 100.

[h] Measure of working memory.

[i] Maximum was 48 points.

[j] Assesses general balance and mobility. Maximum was 12 points.

[k] Assesses general cardiovascular capacity. Due to safety concerns (ie, high resting blood pressure), of the 84 participants who completed the Six-Minute Walk Test at baseline, 68 completed at trial completion (24 for RT, 22 for AT, and 22 for BAT).

ioral associative memory performance (r=0.51; P=.02). The AT group significantly improved general balance and mobility (P=.03) and cardiovascular capacity (P=.04) compared with the BAT group.

Adverse effects included acute episodes of shortness of breath (2 participants) and noninjurious falls (4 participants). There were no significant between-group differences (P = .54) in adverse events.

Comment. In senior women with subjective memory complaints, 6 months of twice-weekly RT improved selective attention/conflict resolution, associative memory, and regional patterns of functional brain plasticity compared with twice-weekly BAT exercises. In contrast, 6 months of twice-weekly AT improved physical function. We provide novel evidence that RT can benefit multiple domains in those at risk for dementia.

While we previously demonstrated that 12 months of twice-weekly RT significantly improved Stroop Test performance in cognitively healthy women 65 to 75 years old,[3] our current study found an improvement after only 6 months in women 70 to 80 years old with probable mild cognitive impairment. Thus, the benefits of RT on selective attention/conflict resolution may be more potent among those at greater risk for dementia.

Baker et al[6] previously demonstrated that 6 months of AT improved selective attention/conflict resolution and set shifting performance in older women with amnestic mild cognitive impairment. This may be attributed to differences in both the frequency and intensity of AT between the 2 studies. In addition, our study participants were older and had lower baseline Mini-Mental State Examination scores.

We also demonstrated that 6 months of RT twice-weekly significantly improved associative memory per-

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formance, co-occurring with positive functional changes in hemodynamic activity in regions involved in the memorization of associations.[10] Impaired associative memory is a hallmark of early stages of Alzheimer disease.

Exercise compliance was low, suggesting that we are providing conservative estimates of the efficacy of RT on cognition and functional plasticity. While the AT group had the highest dropout rate, they demonstrated a significant increase in general cardiovascular capacity. Our findings may not generalize to men or to women of other ages.

In conclusion, our study suggests that twice-weekly RT is a promising strategy to alter the trajectory of cognitive decline in seniors with mild cognitive impairment.

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Primary Care Providers' Response to the US Preventive Services Task Force Draft Recommendations on Screening for Prostate Cancer

In October 2011, the US Preventive Services Task Force (USPSTF) released draft recommendations for prostate cancer screening.[1] Prostate-specific antigen (PSA) testing was given a grade D, indicating that its use for routine screening should be discouraged. The draft recommendations contrast with those of the American Cancer Society and the American Urological Association.[2,3] In the context of competing recommendations and clinical uncertainty, our goals were to examine primary care providers' views of the draft recommendations and to determine to what extent they may be expected to change clinical practice.

Methods. A self-administered written survey was completed by practitioners in a university-affiliated practice, Johns Hopkins Community Physicians (JHCP). The JHCP is composed of 26 outpatient sites in 11 counties in Maryland. In 2010, approximately 40 000 men 40 years and older who were eligible for prostate cancer screening were seen at the JHCP. The survey was distributed at an annual organizational retreat. One hundred forty-one physicians and nurse practitioners who deliver primary care for adult male patients attended the retreat and

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