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Resistance training promotes cognitive and functional brain plasticity in seniors with probable mild cognitive impairment: A 6-month randomized controlled trial

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TO THE EDITOR

Cognitive decline is a pressing health care issue. Worldwide, one new case of dementia is detected every seven 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 and resistance training enhance cognitive performance and functional plasticity in healthy community-dwelling seniors [3–5] and those with mild cognitive impairment [6]. However, 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

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TLA: Study concept and design, acquisition of data, analysis and interpretation of data, preparation of manuscript, and critical review of manuscript. LSN, TCH, CLH, MV: Acquisition of data, analysis and interpretation of data, preparation of manuscript, and critical review of manuscript. All authors had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

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is crucial to utilizing 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 resistance and aerobic training to improve executive cognitive functions – robust predictors of conversion from mild cognitive impairment to Alzheimer's 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

In this six-month randomized trial (EXercise for Cognition and Everyday Living; EXCEL), 86 community-dwelling women aged 70–80 years old were randomly allocated to twice-weekly resistance training (RT; n=28), twice-weekly aerobic training (AT; n=30), or twice-weekly balance and tone training (i.e., control group) (BAT; n=28). Participants were classified as having probable mild cognitive impairment if they scored < 26/30 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. Lastly, 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 6–8 repetitions and loading increased when sets were completed with proper form. The AT program was an outdoor walking program. The training stimulus started at 40% of one's age-specific target heart rate (i.e., heart rate reserve; HRR) and progressed to 70% to 80% of 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 (RT n=26, AT n=24, BAT n=27). Twenty-two participants were included in our fMRI analysis (RT n=7, AT n=7, BAT n=8).

Table 1 shows the baseline characteristics of our sample and change 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=0.04) and the associative memory task (p=0.03). Compared with the BAT group, resistance training also led to functional changes in three regions of cortex -- the right lingual (p=0.03) and occipital-fusiform (p=0.02) gyri, and the right frontal pole (p=0.03) – during the encoding and recall of associations. Additionally, there was a significant positive correlation between change in hemodynamic activity in the right lingual gyrus and change in behavioural associative memory performance (r=0.51; p=0.02). The AT group significantly improved general balance and mobility (p=0.03) and cardiovascular capacity (p=0.04) compared with the BAT group.

Adverse effects included acute episodes of shortness of breath (n=2) and non-injurious falls (n=4). There were no significant between-group differences (p=0.54) in adverse events.

COMMENT

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

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

Baker and colleagues [6] previously demonstrated that six months of aerobic training improved selective attention/conflict resolution and set shifting peformance in older women with amnestic mild cognitive impairment. This may be attributed to differences in both the frequency and intensity of aerobic training between the two studies. Additionally, our study participants were older and had lower baseline MMSE scores.

We also demonstrated six months of resistance training twice-weekly significantly improved associative memory performance, co-occuring 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’s disease.

Exercise compliance was low, suggesting we are providing conservative estimates of the efficacy of resistance training on cognition and functional plasticity. While the aerobic training group had the highest drop out rate, they demonstrated a signficant 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 resistance training is a promising strategy to alter the trajectory of cognitive decline in seniors with mild cognitive impairment.

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Table 1

Baseline characteristics of trial participants and mean change (SDs) for outcome measures at trial completion from baseline (N=86).

Variable [a]	BAT (n=28)	AT (n=30)	RT (n=28)	Total N=86
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Age, years	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 (%)				
Less than Grade 9	0 (0)	2 (2.3)	0 (00	2 (2.3)
Grade 9 to 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[b]	1.0 (1.8)	1.1 (1.8)	1.4 (2.0)	1.2 (1.8)
Functional Comorbidities Index[c]	2.6 (2.2)	2.9 (1.5)	3.0 (1.9)	2.8 (1.8)
Instrumental Activities of Daily Living[d]	7.8 (0.5)	7.8 (0.5)	7.7 (0.8)	7.8 (0.6)
Montreal Cognitive Assessment[e]	27.1 (1.7)	27.4 (1.5)	26.0 (5.6)	22.1 (3.0)
Mini-Mental State Examination[f]	27.1 (1.7)	27.4 (1.5)	26.0 (5.6)	26.8 (3.5)
Exercise Class Compliance[g], %	59 (14.8)	60 (18.7)	54 (14.7)	57 (16.1)
Δ Stroop CW – Stroop C, sec	1.37 (15.26)	8.83 (41.86)	9.13 (19.88)	
Δ Trail B – Trail A[h], sec	−0.39 (40.27)	18.28 (72.55)	−0.91 (43.91)	
Δ Digit Forward – Digit Backward[i]	2.00 (3.14)	0.54 (4.77)	0.73 (2.52)	
Δ Item Memory	0.21 (0.76)	0.55 (1.25)	0.38 (0.75)	
Δ Associative Memory	0.23 (0.66)	−0.09 (0.82)	0.61 (0.72)	
Δ Everyday Problem Solving Test[j]	−1.89 (4.51)	−0.91 (4.46)	−1.40 (5.39)	
Δ Short Physical Performance Battery Score[k]	0.70 (1.77)	1.37 (1.34)	0.40 (1.41)	
Δ Six-Minute Walk Test[l], m	4.50 (34.52)	18.73 (54.63)	11.85 (41.09)	

Abbreviations: BAT=balance and tone; AT=aerobic training; RT=resistance training

[a]Unless otherwise indicated, data are expressed as mean (SD). Percentages (%) have been rounded and may not total 100.

[b]Maximum was 15 points.

[c]Maximum was 18 points.

[d]Maximum was 8 points.

[e]Maximum was 30 points.

[f]Maximum was 30 points.

[g]Calculated as (total number of classes attended/50 classes) × 100.

[h]Measure of set shifting.

[i]Measure of working memory.

[j]Maximum was 48 points.

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

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

[*]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.