Resistance Training and Executive Functions

A 12-Month Randomized Controlled Trial

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Background: Cognitive decline among seniors is a pressing health care issue. Specific exercise training may combat cognitive decline. We compared the effect of once-weekly and twice-weekly resistance training with that of twice-weekly balance and tone exercise training on the performance of executive cognitive functions in senior women.

Methods: In this single-blinded randomized trial, 155 community-dwelling women aged 65 to 75 years living in Vancouver were randomly allocated to once-weekly (n=54) or twice-weekly (n=52) resistance training or twice-weekly balance and tone training (control group) (n=49). The primary outcome measure was performance on the Stroop test, an executive cognitive test of selective attention and conflict resolution. Secondary outcomes of executive cognitive functions included set shifting as measured by the Trail Making Tests (parts A and B) and working memory as assessed by verbal digit span forward and backward tests. Gait speed, muscular function, and whole-brain volume were also secondary outcome measures.

Results: Both resistance training groups significantly improved their performance on the Stroop test compared with those in the balance and tone group ($P \leq .03$). Task performance improved by 12.6% and 10.9% in the once-weekly and twice-weekly resistance training groups, respectively; it deteriorated by 0.5% in the balance and tone group. Enhanced selective attention and conflict resolution was significantly associated with increased gait speed. Both resistance training groups demonstrated reductions in whole-brain volume compared with the balance and tone group at the end of the study ($P \leq .03$).

Conclusion: Twelve months of once-weekly or twice-weekly resistance training benefited the executive cognitive function of selective attention and conflict resolution among senior women.

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COGNITIVE DECLINE AMONG persons 65 years or older (hereinafter seniors) is a pressing health care issue. Effective pharmacologic treatment of mild cognitive impairment and dementia remains a major medical challenge.[1] Hence, effective primary prevention strategies for cognitive decline would greatly benefit individuals and society.

See also pages 124, 179, 186, and 194

Observational studies suggest that physical activity may limit age-associated cognitive decline.[2,3] However, those studies did not distinguish between the 2 main types of physical activity—aerobic and resistance training. Intervention studies have shown that aerobic exercise training enhances brain and cognitive function.[4] Whether resistance training has similar benefits on cognitive function in seniors has received little investigation.[5]

We had 3 reasons to examine whether resistance training improves cognitive function in seniors. First, a meta-analysis[6] highlighted that the greatest benefit of aerobic exercise on cognition occurred when it was paired with resistance training. There are plausible biological mechanisms whereby resistance training might ameliorate cognitive function independently of aerobic exercise.[5] Second, a 6-month trial[7] indicated that resistance training benefited memory performance and verbal concept formation among seniors. This raised the possibility that a broader spectrum of cognitive functions may also show improvement with resis-

tance training. Third, to our knowledge, no study to date has examined the minimum frequency of resistance training (ie, once weekly or twice weekly) required for cognitive benefits. However, the frequency of training may influence long-term exercise adherence. If a relatively standard resistance training program had cognitive benefits and there was evidence of a minimally effective dose (frequency and duration), this would add substantially to physicians' options of exercise prescription for seniors.

We compared the effect of once-weekly and twice-weekly resistance training with twice-weekly balance and tone exercise training on the performance of executive cognitive functions in senior women. We focused on executive cognitive functions because they are highly associated with the ability to perform instrumental activities of daily living[8] and mobility.[9]

METHODS

STUDY DESIGN

We conducted a randomized, controlled 52-week prospective study of exercise from May 1, 2007, through April 30, 2008, with 3 measurement periods (baseline, midpoint, and trial completion). The assessors were blinded to the participants' assignments. However, the success of blinding was not formally assessed throughout the trial.

PARTICIPANTS

The sample consisted solely of women because cognitive response to exercise differs between the sexes.[6] From January 31 to April 30, 2007, we recruited participants with the use of print advertisements and television features. Individuals underwent screening by a standardized telephone interview. Women who lived in Vancouver were eligible for study entry if they (1) were aged 65 to 75 years; (2) were living independently in their own home; (3) scored 24 or more on the Mini-Mental State Examination; and (4) had a visual acuity of at least 20/40, with or without corrective lenses. We excluded those who (1) had a current medical condition for which exercise is contraindicated, (2) had participated in resistance training in the past 6 months, (3) had a neurodegenerative disease and/or a stroke, (4) had depression, (5) did not speak and understand English fluently, (6) were taking cholinesterase inhibitors, (7) were receiving estrogen therapy, or (8) were receiving testosterone therapy.

The CONSORT (Consolidated Standards of Reporting Trials) flowchart in the **Figure** shows the number of participants in the treatment arms at each stage of the study. Ethical approval was obtained from the Vancouver Coastal Health Research Institute and the University of British Columbia's Clinical Research Ethics Board. All participants provided written informed consent.

DESCRIPTIVE VARIABLES

At baseline, participants underwent a physician assessment to confirm current health status and eligibility for the study. We used the 15-item Geriatric Depression Scale[10] to screen for depression. Current level of physical activity was determined by the Physical Activity Scale for the Elderly self-report questionnaire.[11] General mobility was assessed by the timed Up and Go test.[12]

PRIMARY OUTCOME MEASURE

This study focused on the following 3 executive cognitive functions: selective attention and conflict resolution, set shifting, and working memory. Our primary outcome measure was the specific executive cognitive function of selective attention and conflict resolution, as measured by the Stroop test.[13] We previously demonstrated that this function responds to exercise training[14] and used those observed changes in our sample size calculation.

For the Stroop test, we used 3 conditions. First, participants were instructed to read out words printed in black ink (eg, *blue*). Second, they were instructed to read out the color of colored *x*'s. Finally, they were shown a page with color words printed in incongruent colored inks (eg, the word *blue* printed in red ink). Participants were asked to name the ink color in which the words are printed (while ignoring the word itself). There were 80 trials for each condition, and we recorded the time participants took to read each condition. The ability to selectively attend and control response output was calculated as the time difference between the third condition and the second condition. Smaller time differences indicate better selective attention and conflict resolution.

SECONDARY OUTCOME MEASURES

Secondary measures of executive cognitive functions were set shifting and working memory. Also, to understand the wider range of effects resistance training may have on senior women, we assessed gait speed, quadriceps muscular function, and whole-brain volume.

Set Shifting

We used the Trail Making Tests parts A and B to assess set shifting.[15] Part A assesses psychomotor speed and requires the participant to draw lines that connect encircled numbers sequentially, such as drawing a line from 1 to 2, 2 to 3, and 3 to 4. Part B consists of encircled numbers and letters. Participants were instructed to draw a line as quickly and as accurately as possible from 1 to A, A to 2, 2 to B, B to 3, and so on, until they completed the task. We recorded the amount of time (in seconds) it took to complete each task. To index set shifting, we calculated the difference between part B and part A completion times. Smaller difference scores indicate better set shifting.

Working Memory

We used the verbal digit span forward and backward tests to index the central executive component of working memory.[16] Both tests consist of 7 pairs of random number sequences that the assessor reads aloud at the rate of 1 per second. The sequence begins with 3 digits and increases by 1 at a time up to a length of 9 digits. The test includes 2 sequences of each length and testing ceases when the participant fails to recollect any 2 with the same length. The score recorded, ranging from 0 to 14, is the number of successful sequences. For the verbal digit span forward test, the participant's task is to repeat each sequence exactly as it is given. For the verbal digit span backward test, the participant's task is to repeat each sequence in reverse order. The difference between the verbal digit span forward and backward test scores was used as an index of the central executive compo-

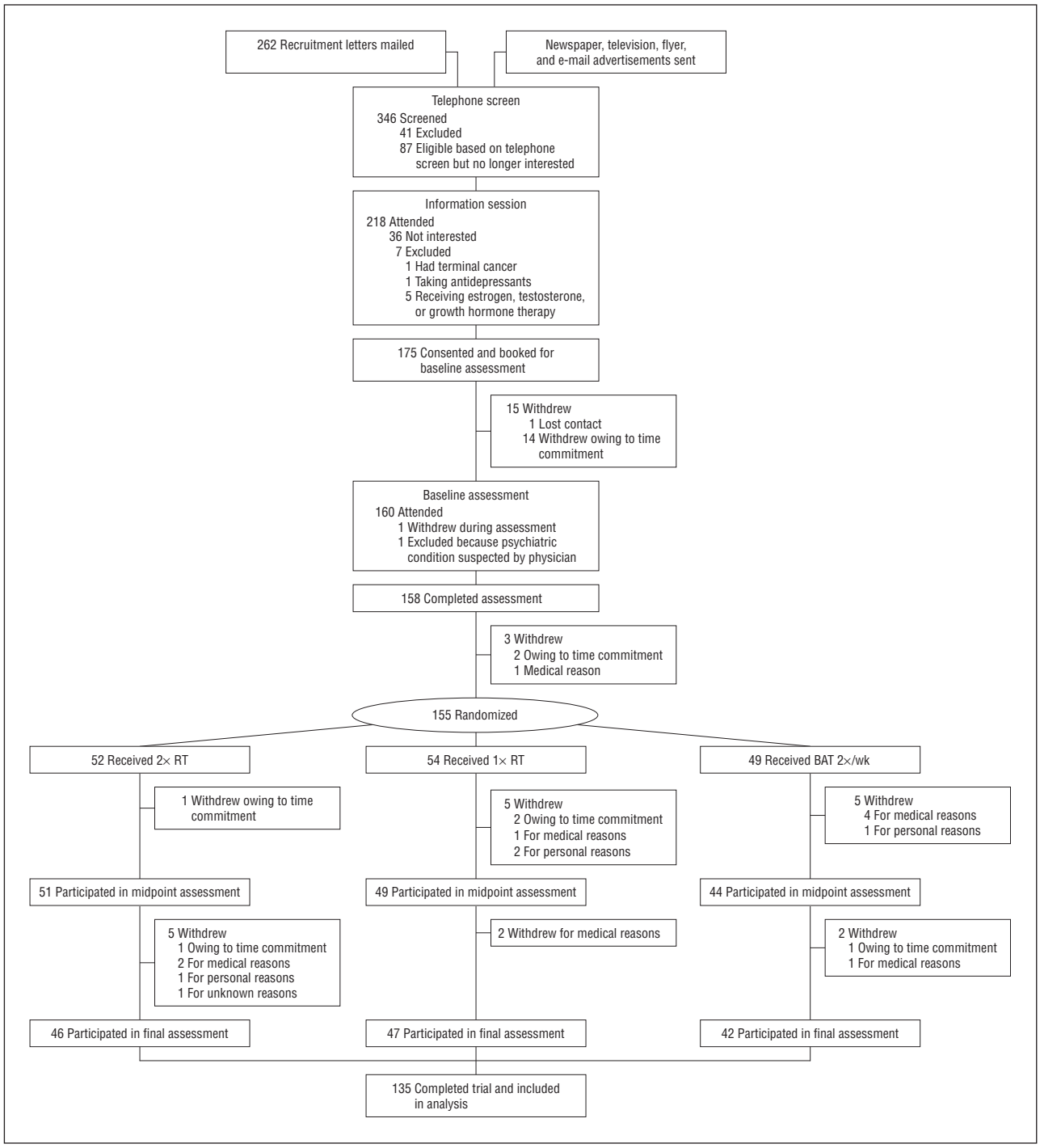

Figure. The CONSORT (Consolidated Standards of Reporting Trials) flowchart. BAT indicates twice-weekly balance and tone exercise training; 1× RT, once-weekly resistance training; and 2× RT, twice-weekly RT.

nent of working memory. Smaller difference scores indicate better working memory.

Gait Speed

Gait speed is a significant and independent predictor of falls and fracture risk in older women.[17] Participants were asked to walk at their usual pace along a 4-m path. Gait speed (in meters per second) was calculated from the mean of 2 trials. The test-retest reliability (intraclass correlation coefficient) of gait speed in our laboratory is 0.95.[18]

Muscular Function

In a subset of participants who were eligible (ie, those with no significant preexisting knee, hip, or back condition), isotonic quadriceps strength (single-repetition maximum lift [1-RM]) and peak muscle power were assessed using an air-pressured digital resistance leg press machine (Keiser Sports Health Equipment, Fresno, California). The study physician screened all participants for eligibility. Two assessors completed all assessments of 1-RM and peak muscle power; they attended two

30-minute training sessions before the baseline measurement period.

The initial load for quadriceps 1-RM assessment was the participant's own body mass. Participants pushed against the leg press over a 3-second count and then returned to the start position over a 3-second count. Load increased by 10% increments until participants were no longer able to lift the load through their available range of motion. The load (in newtons) of the last successfully completed leg press was recorded and used for statistical analysis.

After the completion of the quadriceps 1-RM testing, eligible participants were given a 15-minute break. They then underwent quadriceps muscle power assessments during which they completed leg press extensions at 6 relative loads of their 1-RM (ie, 40%, 50%, 60%, 70%, 80%, and 90%). Participants performed the concentric portion of the leg press repetition as rapidly as possible and then slowly lowered the load during a 3-second count. Beginning at 40% of 1-RM, participants performed 3 repetitions at each relative 1-RM load. There was a 30-second rest between repetitions. The air-pressured digital resistance leg press machine recorded the power produced (in watts). The peak quadriceps muscle power obtained by each participant was used for statistical analysis.

Whole-Brain Volume

For those who met the inclusion criteria for magnetic resonance imaging and consented, whole-brain volume was measured via T1-weighted structural magnetic resonance images obtained using a 3T scanner (Achieva; Philips Medical Systems UK Ltd, Surrey, England). Calculations of whole-brain volume and their percentage change across study time points were made using the SIENA (Structural Image Evaluation, using Normalization, of Atrophy) method of automated analysis.[19] SIENA is a longitudinal method that compares pairs of scans within subjects and is available as part of the Functional Magnetic Resonance Imaging of the Brain Software Library package.[20] SIENA has been shown to have an overall error rate of approximately 0.2% of the absolute brain volume.[19,21,22] It is designed to be fully automatic, but careful evaluation of its intermediate output is essential to ensuring accurate results. To minimize error, we performed visual checks of intermediate output from 3 critical processes: brain extraction, spatial alignment, and tissue segmentation.

RANDOMIZATION

The randomization sequence was generated by http://www.randomization.com and was concealed until interventions were assigned. This sequence was held independently and remotely by the research coordinator. Participants were enrolled and randomized by the research coordinator to one of the following 3 groups: once-weekly resistance training (1×RT), twice-weekly resistance training (2×RT), or twice-weekly balance and tone (BAT).

SAMPLE SIZE

The required sample size for this study was calculated from predictions of 12-month changes in the Stroop test results. Specifically, we predicted a 6% improvement for the 1×RT and a 12% improvement for the 2×RT groups. We also estimated a 10% deterioration in the BAT group (ie, the control group). These estimates were based on our previous work,[14] which demonstrated that a home-based program of strength and balance retraining exercises significantly improved Stroop test performance. Assuming a 20% attrition rate and using an α level of less than .05, 52 participants per group ensured a power of 0.80.

EXERCISE INTERVENTION

The resistance training and balance and tone classes both began 1 month after the baseline assessments were completed (ie, May 2007). Classes were held at 2 locations: the local YMCA and the Centre for Hip Health and Mobility research center. All classes were led by certified fitness instructors who received additional training and education from the study investigators. The classes were 60 minutes long, with a 10-minute warm-up, 40 minutes of core content, and a 10-minute cooldown. To ensure that programs were delivered faithfully and consistently across sites, a research assistant who was not involved in delivering the study's classes conducted quality assessments every month with the use of a standard form. Attendance was recorded daily by the assistants. Adherence, expressed as the percentage of the total number of classes attended, was calculated from these attendance sheets.

Specific strategies were implemented to promote participant engagement. These included (1) semimonthly newsletters that featured personal accomplishments of the participants, healthy recipes contributed by the participants, and study updates; (2) 3 social events (eg, the Winter Holiday Tea); (3) personalized birthday cards; (4) follow-up for participants who missed 2 consecutive classes without a reason; and (5) support and suggestions for overcoming barriers to participation.

Resistance Training

The resistance training program used a progressive, high-intensity protocol. The air-pressured digital resistance leg press machine and free weights were used to provide the training stimulus. The leg press machine–based exercises consisted of biceps curls, triceps extension, seated rowing, latissimus dorsi pull-down exercises, leg presses, hamstring curls, and calf raises. The intensity of the training stimulus was at a work range of 6 to 8 repetitions (2 sets). The training stimulus was subsequently increased using the 7-RM method, when 2 sets of 6 to 8 repetitions were completed with proper form and without discomfort. Other key strength exercises included minisquats, minilunges, and lunge walks. The number of sets completed and the load lifted for each exercise were recorded for each participant at every class.

Balance and Tone

The balance and tone program consisted of stretching exercises, range-of-motion exercises, basic core-strength exercises including kegels (ie, exercises to strengthen the pelvic floor muscles), balance exercises, and relaxation techniques. Key balance exercises included tai chi–based forms (ie, the crane and the tree pose), tandem stand, tandem walking, and single leg stance (eyes opened and closed). Other than body weight, no additional loading (eg, hand weights or resistance bands) was applied to any of the exercises. There is no evidence that these exercises improve cognitive function.[4] This group served to control for confounding variables such as physical training received by traveling to the training centers, social interaction, and changes in lifestyle secondary to study participation.

ADVERSE EFFECTS

Participants were questioned about the presence of any adverse effects, such as musculoskeletal pain or discomfort, at each exercise session. All instructors also monitored participants for

Table 1. Baseline Characteristics of the 155 Trial Participants[a]

Variable	Group			
	BAT (n=49)	1× RT (n=54)	2× RT (n=52)	All (N=155)
Age, y	70.0 (3.3)	69.5 (2.7)	69.4 (3.0)	69.6 (2.9)
Height, cm	161.0 (6.9)	160.9 (7.0)	162.8 (6.5)	161.6 (6.8)
Weight, kg	67.0 (11.5)	69.2 (16.2)	72.1 (16.8)	69.5 (15.2)
Education, No. (%)				
No high school	1 (2.0)	1 (1.9)	1 (1.9)	**3** (1.9)
Grades 9-12 without certificate or diploma	2 (4.1)	3 (5.6)	4 (7.7)	**9** (5.8)
High school certificate or diploma	6 (12.2)	9 (16.7)	10 (19.2)	**25** (16.1)
Trade or professional certificate or diploma	14 (28.6)	10 (18.5)	6 (11.5)	**30** (19.4)
University certificate or diploma	7 (14.3)	12 (22.2)	9 (17.3)	**28** (18.1)
University degree	19 (38.8)	19 (35.2)	22 (42.3)	**60** (38.7)
MMSE score[b]	28.8 (1.2)	28.5 (1.3)	28.6 (1.5)	28.6 (1.3)
Falls in the last 12 months, No. (%)	16 (32.7)	13 (24.1)	20 (38.5)	**49** (31.6)
Geriatric Depression Scale[c]	0.5 (1.8)	0.3 (1.1)	0.9 (2.3)	0.6 (1.8)
Functional Comorbidity Index[d]	2.2 (1.7)	1.8 (1.7)	2.3 (1.6)	2.1 (1.7)
Lawton and Brody Instrumental Activities of Daily Living Scale score[e]	8.0 (0)	8.0 (0.1)	7.9 (0.5)	8.0 (0.3)
PASE score	126.1 (51.0)	116.2 (61.4)	121.2 (60.4)	121.0 (57.7)
TUG, s	6.8 (1.4)	6.6 (1.4)	6.6 (1.4)	6.6 (1.4)

Abbreviations: BAT, balance and toning; MMSE, Mini-Mental State Examination; PASE, Physical Activity Scale for the Elderly; TUG, timed Up and Go test; 1× RT, once-weekly resistance training; 2× RT, twice-weekly RT.

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

[b] Maximum was 30 points.

[c] Maximum was 15 points.

[d] Maximum was 18 points.

[e] Maximum was 8 points. The scale is described in Lawton and Brody.[29]

symptoms of angina and shortness of breath during the exercise classes.

STATISTICAL ANALYSIS

All analyses were full analysis set,[23] defined as the analysis set that is as complete and as close as possible to the intention-to-treat ideal of including all randomized participants. Data were analyzed using SPSS statistical software (Windows version 17.0; SPSS Inc, Chicago, Illinois).

Between-group differences in selective attention and conflict resolution at the midpoint and at trial completion were compared by multiple linear regression analysis. In the models, baseline scores, experimental group, baseline Mini-Mental State Examination score, baseline waist circumference,[24,25] diagnosis of diabetes (yes/no),[25-27] and visual edge contrast sensitivity score[28] were included as covariates. Two planned simple contrasts were performed when there were significant main group effects. These contrasts were used to assess differences between the 1× RT group and the BAT group and between the 2× RT group and the BAT group. In addition, difference contrasts were used within each RT group to assess when cognitive benefits of resistance training were evident. The overall α level was set at $P < .05$.

We analyzed our secondary outcome measures of executive cognitive functions in the same manner as our primary outcome measure with the exception that visual edge contrast sensitivity was not included as a covariate in the model for working memory.

For models of gait speed, quadriceps 1-RM, and peak quadriceps muscle power, baseline scores and experimental group were included as covariates. For models of percentage of change in whole-brain volume, presence of diabetes was included as a covariate. Finally, Pearson product moment correlations were computed to determine whether changes in selective attention and conflict resolution between the beginning and the end of the intervention period were related to changes in gait speed.

RESULTS

DESCRIPTIVE VARIABLES, EXERCISE ADHERENCE, AND PHYSICAL ACTIVITY LEVELS

The mean (SD) age of the cohort was 69.6 (2.9) years, and the exercise adherence during the 1-year study period was 67.9%. Average adherence was 71.0% for the 1× RT group, 70.3% for the 2× RT group, and 62.0% for the BAT group. Baseline demographics and characteristics of the 155 participants who were randomized are shown in **Table 1**. Physical activity levels (Physical Activity Scale for the Elderly scores) did not differ significantly between the groups at the midpoint ($P = .98$) or at trial completion ($P = .68$).

PRIMARY OUTCOME MEASURE

Table 2 shows the baseline, midpoint, and trial completion results for the executive cognitive function tests. The regression analyses revealed no significant between-group differences at the midpoint of the trial. However, at the end of the trial, there was a significant between-group difference in selective attention and conflict resolution ($P = .01$). Planned simple contrasts indicated that both the 1× RT and 2× RT groups had improved Stroop test performance compared with the BAT group at trial completion ($P \leq .03$). Specifically, task performance improved by 12.6% and 10.9% in the 1× RT and 2× RT

Table 2. Mean Values for Outcome Measures

Variable	Mean (SD)		
	Baseline	Midpoint	Completion
2× RT group	**n=52**	**n=51**	**n=46**
Stroop test, CW – C, s	45.0 (15.8)	46.1 (17.2)	40.9 (14.9)[a]
Trail Making Test, part B – part A, s	49.5 (36.6)	41.7 (30.8)	38.7 (33.6)
Verbal digit span test, forward – backward	3.4 (2.4)	4.1 (2.9)	3.8 (2.1)
Gait speed, m/s	1.2 (0.2)	1.3 (0.2)	1.4 (0.2)
1-RM, N[b]	315.0 (66.9)	380.6 (84.0)	388.2 (82.4)
Peak muscle power, W[c]	624.9 (194.2)	707.2 (171.6)[a]	708.6 (161.2)[a]
Change in whole-brain volume from baseline, %[d]	NA	–0.02 (0.60)	–0.43 (0.65)[a]
1× RT group	**n=54**	**n=49**	**n=47**
Stroop test, CW – C, s	47.4 (26.2)	46.5 (25.8)	39.5 (14.1)[a]
Trail Making Test, part B – part A, s	41.4 (26.5)	36.1 (27.8)	34.0 (27.4)
Verbal digit span test, forward – backward	3.5 (2.0)	3.8 (2.3)	3.4 (1.9)
Gait speed, m/s	1.2 (0.2)	1.4 (0.2)	1.4 (0.2)
1-RM, N[b]	323.9 (63.2)	371.0 (86.4)	386.5 (97.0)
Peak muscle power, W[c]	679.3 (184.2)	633.4 (192.3)	622.3 (204.4)
Change in whole-brain volume from baseline, %[d]	NA	–0.04 (0.48)	–0.32 (0.54)[a]
BAT group	**n=49**	**n=44**	**n=42**
Stroop test, CW – C, s	44.0 (15.1)	49.2 (19.1)	43.8 (18.9)
Trail Making Test, part B – part A, s	47.1 (41.3)	43.4 (28.8)	36.0 (21.9)
Verbal digit span test, forward – backward	3.2 (2.5)	4.4 (2.8)	4.0 (1.9)
Gait speed, m/s	1.2 (0.2)	1.3 (0.2)	1.4 (0.2)
1-RM, N[b]	338.2 (70.4)	363.9 (77.4)	356.3 (85.3)
Peak muscle power, W[c]	660.3 (229.7)	649.5 (208.8)	552.1 (194.0)
Change in whole-brain volume from baseline, %[d]	NA	0.13 (0.67)	0.00 (0.63)

Abbreviations: BAT, balance and toning; C, Stroop test colored *x*'s condition; CW, Stroop test color words condition; NA, not applicable; 1-RM, isotonic quadriceps strength; 1× RT, once-weekly resistance training; 2× RT, twice-weekly RT.

[a] Significantly different from the BAT group at $P < .05$. For the Stroop test, the 95% confidence interval (CI) of the difference between the 1× RT and BAT groups was –13.8 to –2.5; between the 2× RT and BAT groups, –12.2 to –0.8. For peak muscle power, 95% CI of the difference between the 2× RT and BAT groups at the midpoint was 22.2 to 151.3; between the 2× RT and BAT groups at trial completion, 81.7 to 230.0. For the difference in whole-brain volume, the 95% CI of the difference between the 1× RT and BAT groups was –0.76 to –0.04; between the 2× RT and BAT groups, –0.89 to –0.12.

[b] For this analysis, 31 participants were included in the 2× RT group at baseline, 26 at the midpoint, and 25 at trial completion; in the 1× RT group, 30 at baseline, 28 at the midpoint, and 27 at trial completion; and in the BAT group, 27 at baseline, 21 at the midpoint, and 24 at trial completion.

[c] For this analysis, 30 participants were included in the 2× RT group at baseline, 23 at the midpoint, and 25 at trial completion; in the 1× RT group, 29 at baseline, 26 at the midpoint, and 27 at trial completion; and in the BAT group, 27 at baseline, 21 at the midpoint, and 24 at trial completion.

[d] For the 2× RT group, 18 participants were included in the differences from baseline to the midpoint and from baseline to trial completion; for the 1× RT group, 28 in the differences from baseline to the midpoint and from baseline to trial completion; for the BAT group, 20 in the difference from baseline to the midpoint and 18 from baseline to trial completion.

groups, respectively, whereas the BAT group demonstrated a 0.5% deterioration. Within each RT group, difference contrasts demonstrated that Stroop test performance was not significantly different from baseline to the midpoint ($P = .79$), but was significantly different from the midpoint to trial completion ($P = .001$).

SECONDARY OUTCOME MEASURES

The regression analyses revealed no significant between-group differences at the midpoint and at trial completion in set shifting and working memory (Table 2).

There were no significant between-group differences at the midpoint and at trial completion in gait speed and quadriceps 1-RM. However, there were significant between-group differences in peak muscle power at the midpoint ($P < .01$) and at trial completion ($P < .001$). Planned simple contrasts indicated that the 2× RT group increased peak muscle power at the midpoint ($P < .01$) and at trial completion ($P < .001$) compared with the BAT group. Specifically, at trial completion, peak muscle power increased by 13.4% in the 2× RT group but decreased by 8.4% and 16.3% for the 1× RT and BAT groups, respectively.

There were also between-group differences in the percentage of change of whole-brain volume at trial completion ($P \leq .03$) (**Table 3**). At the end of the study, the 1× RT and 2× RT groups both demonstrated reductions in whole-brain volume compared with the BAT group ($P \leq .03$). Specifically, there was a 0.32% and a 0.43% reduction in whole-brain volume for the 1× RT and 2× RT groups, respectively. In contrast, there was no change in whole-brain volume for the BAT group.

Improvement in selective attention and conflict resolution during the 12-month intervention was significantly associated with improvement in gait speed ($r = 0.24$; $P < .01$).

ADVERSE EVENTS

Results of the χ^2 test indicated significant group differences ($P = .02$) in the proportion of participants reporting adverse events. Specifically, musculoskeletal complaints (eg, knee joint discomfort or bursa irritation in the lateral hip) developed in 14 of 47 women (29.8%) in the 1× RT group, in 5 of 46 (10.9%) in the 2× RT group, and in 4 of 42 (9.5%) in the BAT group. All documented

Table 3. Mean Change for Outcome Measures

Variable	Mean (SD) Change[a]	
	Midpoint	Completion
2× RT group	**n=51**	**n=46**
Stroop test, CW – C, s	–0.96 (15.13)	5.01 (13.75)
Trail Making Test, part B – part A, s	10.27 (40.25)	10.96 (36.92)
Verbal digit span test, forward – backward	–0.67 (2.94)	–0.47 (2.24)
Gait speed, m/s	0.19 (0.17)	0.24 (0.16)
1-RM, N[b]	60.27 (51.18)	69.80 (74.75)
Peak muscle power, W[c]	74.68 (118.55)	72.42 (108.12)
Change in whole-brain volume, %[d]	–0.02 (0.60)	–0.43 (0.65)
1× RT group	**n=49**	**n=47**
Stroop test, CW – C, s	0.28 (28.37)	6.22 (22.31)
Trail Making Test, part B – part A, s	4.91 (26.12)	7.3 (30.36)
Verbal digit span test, forward – backward	–0.43 (2.63)	0.06 (2.54)
Gait speed, m/s	0.18 (0.19)	0.19 (0.19)
1-RM, N[b]	42.15 (57.26)	44.22 (67.10)
Peak muscle power, W[c]	–27.54 (105.66)	–78.61 (151.03)
Change in whole-brain volume, %[d]	–0.04 (0.48)	–0.32 (0.54)
BAT group	**n=44**	**n=42**
Stroop test, CW – C, s	–4.27 (15.15)	0.26 (17.12)
Trail Making Test, part B – part A, s	2.17 (39.27)	8.64 (32.15)
Verbal digit span test, forward – backward	–0.93 (3.42)	–0.64 (2.70)
Gait speed, m/s	0.17 (0.16)	0.22 (0.18)
1-RM, N[b]	24.73 (53.44)	18.15 (70.06)
Peak muscle power, W[c]	–24.27 (132.56)	–90.60 (144.58)
Change in whole-brain volume, %[d]	0.13 (0.67)	0.00 (0.63)

Abbreviations: See Table 2.

[a] Mean change for all cognitive measures is calculated as the difference between the baseline value and the midpoint or the completion value. Positive change indicates improvement. Mean change for all performance measures is calculated as the difference between the midpoint and baseline values or between the completion and baseline values. Positive change indicates improvement.

[b] For this analysis, 31 participants were included in the 2× RT group at baseline, 26 at the midpoint, and 25 at trial completion; in the 1× RT group, 30 at baseline, 28 at the midpoint, and 27 at trial completion; and in the BAT group, 27 at baseline, 21 at the midpoint, and 24 at trial completion.

[c] For this analysis, 30 participants were included in the 2× RT group at baseline, 23 at the midpoint, and 25 at trial completion; in the 1× RT group, 29 at baseline, 26 at the midpoint, and 27 at trial completion; and in the BAT group, 27 at baseline, 21 at the midpoint, and 24 at trial completion.

[d] For the 2× RT group, 18 participants were included in the differences from baseline to the midpoint and from baseline to trial completion; for the 1× RT group, 28 in the differences from baseline to the midpoint and from baseline to trial completion; and for the BAT group, 20 in the difference from baseline to the midpoint and 18 from baseline to trial completion.

musculoskeletal symptoms resolved or diminished within 4 weeks of onset. There was also 1 fall in the BAT group; this fall did not result in injury.

COMMENT

In community-dwelling women aged 65 to 75 years, 12 months of progressive resistance training once or twice weekly improved selective attention and conflict resolution relative to twice-weekly balance and toning exercises. We also found that resistance training twice weekly improved peak quadriceps muscle power, and that resistance training once or twice weekly led to small but significant reductions in whole-brain volume. To our knowledge, this is the first study to demonstrate that engaging in progressive resistance training as infrequently as once a week can significantly benefit executive cognitive function in community-dwelling senior women.

Cassilhas et al[7] demonstrated that 6 months of thrice-weekly moderate- or high-intensity resistance training improved cognitive performance of memory and verbal concept formation among senior men. Our findings extend these results in several critical ways. Most notably, our results suggest that the effects of resistance training on executive cognitive functions appear to be selective; that is, resistance training enhanced selective attention and conflict resolution in older women, but cognitive abilities associated with manipulating verbal information in working memory and shifting between task sets or instructions were not improved.

Our study provides novel data relating the frequency and duration of resistance training with cognitive benefits in women. We observed a cognitive benefit after 12 months of training but not at the 6-month trial midpoint. Cassilhas et al[7] reported cognitive benefits after 6 months of resistance training in men. There were differences in the frequency of resistance training between the 2 studies (ie, once-weekly and twice-weekly training in our study vs thrice-weekly training in the Brazilian study); also, different cognitive functions may have different change trajectories with resistance training. Sex may also be a moderating factor. Our study included women only, and the participants trained less frequently than did those in the study by Cassilhas et al.[7] Finally, differences in the control groups may have contributed to the lack of between-group differences in cognitive performance at 6 months. The control group in the Brazilian study[7] trained only once weekly; our Canadian control group trained twice weekly.

We also demonstrated that enhanced selective attention and conflict resolution was associated with increased gait speed. To our knowledge, this study is the first to demonstrate this relationship. Our finding adds weight to previous observations of a strong relationship between gait speed and cognitive function.[30] The implication for clinicians is that improved gait speed is a predictor of substantial reduction in mortality.[31]

The design of our control group (ie, balance and toning) may have also contributed to the lack of between-group differences at 6 and 12 months in quadriceps 1-RM. Our control group included balance training in their twice-weekly program. Previous studies have demonstrated that balance training exercises can improve muscle strength.[32,33] In addition, in our own previous investigation of different types of exercise training (ie, resistance training, agility training, and stretching [ie, control] exercises) in senior women with low bone mass, we did not find any significant between-group differences in measures of quadriceps strength and mobility.[34]

We highlight that, although both resistance training groups enhanced selective attention and conflict resolution by the end of the trial, there were more musculoskeletal adverse events in the 1×RT group than in the 2×RT and BAT groups. Hence, the possible increased risk for musculoskeletal injury with once-weekly resistance training must be weighed against its benefit of re-

duced training time compared with twice-weekly resistance training.

An unexpected result was the reduced whole-brain volume for both RT groups. Although reduced brain volumes are commonly associated with impaired function,[35] the groups who improved cognitive executive function and muscular function in our study also had brain volume reductions. There are precedents that parallel our apparently paradoxical finding.[36,37] In a β-amyloid immunization trial among those with probable Alzheimer disease, immunization led to significant clinical benefit, reduced β-amyloid load, and reduced brain volume.[36] The investigators hypothesized that removal of β-amyloid and/or other protein constituents from brain tissue may have caused cerebral fluid shifts, resulting in brain volume reductions on magnetic resonance imaging. However, we are very cautious in our interpretation of the whole-brain volume results and emphasize that this facet of the study, although not the first report of such a phenomenon, needs further investigation.

Because our participant sample included women aged 65 to 75 years only, the findings may not generalize to men or to women of other ages. Also, although we observed reduced whole-brain volumes, the study was not designed to show which specific brain regions demonstrated volumetric changes.

In conclusion, we provide novel randomized controlled trial evidence that a pragmatic resistance training program can enhance the executive cognitive function of selective attention and conflict resolution and simultaneously improve muscular function in senior women. This has important clinical implications because cognitive impairment is a major health problem that currently lacks a clearly effective pharmaceutical therapy and because resistance training is not widely adopted by seniors. The doses of resistance training we used in this study fall within those recommended by the 2008 Physical Activity Guidelines for seniors.[38]

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Author Contributions: Dr Liu-Ambrose had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Liu-Ambrose, Nagamatsu, Graf, Beattie, and Handy. *Acquisition of data:* Liu-Ambrose, Nagamatsu, Ashe, and Handy. *Analysis and interpretation of data:* Liu-Ambrose, Nagamatsu, Graf, Beattie, and Handy. *Drafting of the manuscript:* Liu-Ambrose, Nagamatsu, Graf, and Handy. *Critical revision of the manuscript for important intellectual content:* Liu-Ambrose, Nagamatsu, Beattie, Ashe, and Handy. *Statistical analysis:* Liu-Ambrose and Handy. *Obtained funding:* Liu-Ambrose and Graf. *Administrative, technical, and material support:* Liu-Ambrose, Nagamatsu, Beattie, Ashe, and Handy. *Study supervision:* Liu-Ambrose and Handy.
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