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Neurobiology of Aging xx (2011) xxx

NEUROBIOLOGY OF AGING

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Resistance training and functional plasticity of the aging brain: a 12-month randomized controlled trial

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Received 6 July 2010; received in revised form 11 May 2011; accepted 15 May 2011

Abstract

Maintaining functional plasticity of the cortex is essential for healthy aging and aerobic exercise may be an effective behavioral intervention to promote functional plasticity among seniors. Whether resistance training has similar benefits on functional plasticity in seniors has received little investigation. Here we show that 12 months of twice-weekly resistance training led to functional changes in 2 regions of cortex previously associated with response inhibition processes—the anterior portion of the left middle temporal gyrus and the left anterior insula extending into lateral orbital frontal cortex—in community-dwelling senior women. These hemodynamic effects co-occurred with improved task performance. Our data suggest that resistance training improved flanker task performance in 2 ways: (1) an increased engagement of response inhibition processes when needed; and (2) a decreased tendency to prepare response inhibition as a default state. However, we highlight that this effect of resistance training was only observed among those who trained twice weekly; participants of the once-weekly resistance training did not demonstrate comparable response profiles, both in behavioral performance and hemodynamic activity in cortex. In sum, our findings suggest that twice-weekly resistance training in seniors can positively impact functional plasticity of response inhibition processes in cortex, and that it does so in a manner that complements the effects on selective attention that have previously been ascribed to aerobic exercise in seniors.

Keywords: Resistance training; Functional plasticity; Older women

1. Introduction

The world's population is aging—at a rate that is unprecedented in human history. Maintaining functional plasticity of the cortex is essential for healthy aging, but how can this be promoted at a population level? One promising approach is exercise, which comes in 2 distinct forms—aerobic training, such as running, and resistance training, such as lifting weights. In rats, aerobic exercise training increased levels of brain-derived neurotrophic factors (Neeper et al., 1995) which, in turn, increased neuronal survival, synaptic development, and plasticity (Barde, 1994; Cotman and Engesser-Cesar, 2002; Lu and Chow, 1999). Neuroanatomical studies show that these central benefits of aerobic exercise training are also found in older adults and were most evident in cortical regions that typically show the greatest age-related declines (Colcombe et al., 2003, 2004). However, aerobic exercise training requires relatively healthy joints and a degree of cardiovascular fitness; both of these can be limited in seniors.

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doi:10.1016/j.neurobiolaging.2011.05.010

In comparison, resistance training is a familiar form of exercise for many Baby Boomers and it is feasible even for those with limited mobility or cardiovascular fitness. Two studies to date have demonstrated the beneficial effect of progressive resistance training on cognitive performance among older adults (Cassilhas et al., 2007; Liu-Ambrose et al., 2010). Specifically, Cassilhas (2007) demonstrated that 6 months of either thrice-weekly moderate- or high-intensity resistance training improved cognitive performance of memory and verbal concept formation among senior men. We recently demonstrated that 12 months of progressive resistance training once- or twice-weekly improved selective attention and conflict resolution, relative to twice-weekly balance and toning exercises in senior women. However, whether resistance training affects functional plasticity is currently unknown.

Studies with intermediate outcome measures from both human trials and laboratory experiments justify examination of resistance training and functional plasticity. In humans, resistance training reduced serum homocysteine (Vincent et al., 2003) and increased levels of insulin-like growth factor 1 (IGF-1) (Borst et al., 2001; Cassilhas et al., 2007). Increased homocysteine levels are associated with impaired cognitive performance (Schafer et al., 2005), Alzheimer's disease (Seshadri et al., 2002), and cerebral white matter lesions (Vermeer et al., 2002). In rat models, elevated levels of homocysteine are neurotoxic (Kruman et al., 2000). In contrast, IGF-1 promotes neuronal growth, survival, and differentiation and improves cognitive performance (Cotman and Berchtold, 2002).

If resistance training had similar, or complementary, positive effects on functional plasticity as aerobic exercise training, it would allow a greater portion of the aging population to utilize another powerful exercise intervention strategy with multiple benefits. Based on the previous work of Colcombe and colleagues (2004) on aerobic exercise training and cortical functioning associated with selective attention and conflict resolution, we hypothesize that resistance training will increase activation in the frontal and parietal cortices—specifically, the middle frontal gyrus, superior frontal gyrus, and superior parietal lobe—and will reduce activation in the anterior cingulate cortex. However, given that no previous studies have examined the potential effect of resistance training on cortical functioning associated with selective attention and conflict resolution, it is possible that we will identify nonoverlapping regions of the brain. Here we report the results of a 12-month randomized controlled trial that suggest that twice-weekly resistance training produces positive effects on functional plasticity among community-dwelling senior women.

2. Methods

2.1. Study design

We conducted a randomized, controlled 52-week prospective study of exercise from May 2007 to April 2008. The assessors were blinded to the participants' assignments.

2.2. Participants

The sample has been described in detail previously (Liu-Ambrose et al., 2010). Briefly, women who lived in Vancouver, Canada, were eligible for study entry if they: (1) were aged 65 to 75 years; (2) were living independently in their own home; (3) scored $\geq$ 24 on the Mini Mental State Examination (MMSE); 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 last 6 months; (3) had a neurodegenerative disease and/or stroke; (4) had depression; (5) did not speak and understand English fluently; (6) were taking cholinesterase inhibitors; (7) were using estrogen replacement therapy; or (8) were using testosterone therapy. 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.

2.3. Randomization

The randomization sequence was generated by www.randomization.com and was concealed until interventions were assigned. This sequence was held independently and remotely by the study research coordinator. Participants were enrolled and randomized by the research coordinator to 1 of 3 groups: once-weekly resistance training (RT1), twice-weekly resistance training (RT2), or twice-weekly balance and tone training (BAT).

2.4. Exercise intervention

The exercise classes began 1 month after the baseline assessments were completed (i.e., May 2007). A detailed description of these classes has been previously reported (Liu-Ambrose et al., 2010). We provide a brief description here. Attendance was recorded daily by the assistants. Compliance, expressed as the percentage of the total classes attended, was calculated from these attendance sheets.

2.4.1. Resistance training

The protocol for both resistance training programs (RT1 and RT2) was progressive in loading. Both a Keiser Pressurized Air System (Keiser, Fresno, CA, USA) and free weights were used to provide the training stimulus. 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 7RM 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.

2.4.2. Balance and tone

The BAT program consisted of stretching exercises, range of motion exercises, basic core strength exercises including kegals, balance exercises, and relaxation techniques. 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.

2.5. 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 (GDS) (Yesavage, 1988) to screen for depression. Current level of physical activity was determined by the Physical Activities Scale for the Elderly (PASE) self-report questionnaire (Washburn et al., 1999). General mobility was assessed by the Timed Up and Go Test (TUG) (Podsiadlo and Richardson, 1991).

2.6. Functional magnetic resonance imaging (fMRI) data acquisition

Data were acquired on a 3T Intera Achieva MRI scanner (Philips Medical Systems Canada, Markham, Ontario, Canada) in the UBC, High Field MRI Centre at the UBC Hospital. Transverse echo-planar imaging (EPI) images inplane with the anterior and posterior commissure (AC-PC) line were acquired using a gradient-echo pulse sequence and sequential slice acquisition (repetition time [TR] = 2000 ms, echo time [TE] = 30 ms, flip angle = 90°, 36 contiguous slices at 3 mm skip 1 mm, in-plane resolution of 128 × 128 pixels reconstructed in a field of view of 240 mm). Each functional run began with 4 TR's during which no data were acquired to allow for steady-state tissue magnetization. A total of 148 echo-planar imaging volumes were collected in each functional run, and a total of 6 functional runs were collected for each participant. High-resolution, T1-weighted axial images were also taken of each participant (TR = 8 ms, TE = 3.7 ms, bandwidth = 2.26 kHz, voxel size = 1 × 1 × 1 mm).

During scanning, participants performed a modified Eriksen flanker task (Colcombe et al., 2004)—a task that engages both selective attention and conflict resolution (Fig. 1). Participants viewed displays with a central arrow cue flanked by a pair of arrows on either side. In half the trials, the flanking arrows pointed in the same direction as the central arrow cue (e.g., < < < < <; congruent condition), and in the other half, the flanking arrows pointed in the opposite direction (e.g., > > < > >; incongruent condition). The participants' task on each trial was to signal the direction the central arrow points via a simple key press.

2.7. Behavioral analysis

The primary behavioral outcome was computed as the percentage increase in reaction time to incongruent stimuli, over and above the average reaction time to congruent stimuli {[(incongruent reaction time − congruent reaction time)/congruent reaction time] × 100} (Colcombe et al., 2004). The percentage increase measure is derived to reflect

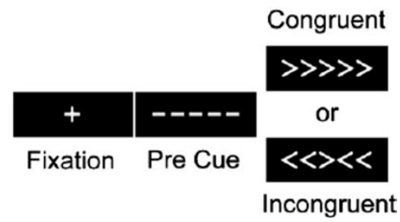

Fig. 1. Erikson flanker task. Each trial began with a 13.5-second fixation cross, followed by a 500-millisecond precue to inform participants that the critical stimulus was about to appear. Finally, 5 arrows were presented and participants were required to respond to the orientation of the central arrow by pressing 1 button with their left hand if the arrow pointed to the left, and another button with their right hand if the arrow pointed to the right. Half of the trials were congruent, where the flanking arrows pointed in the same direction as the central arrow. The other half of the trials were incongruent, where the flanking arrows pointed in the opposite direction of the central arrow. The arrows remained on the screen for 2000 milliseconds. There were equal numbers of trials with the arrows pointing left and right. Each block consisted of 16 trials and was approximately 5 minutes long, with each participant completing 6 blocks total.

interference unbiased by differences in base reaction time. Only correct responses were included in analysis. We compared the change in the interference scores between groups by 2 planned simple contrasts with an overall alpha level of $p < 0.05$. These contrasts were employed to assess differences between: (1) the RT1 group and the BAT group; and (2) the RT2 group and the BAT group.

2.8. fMRI data processing and analysis

Data were preprocessed using FEAT (Version 5.98), which is part of FSL (FMRIB's Software Library, Version 4.1.4; FMRIB Analysis Group, Oxford University, UK). Data were motion corrected (Jenkinson, 2003), registered by FLIRT (Jenkinson and Smith, 2001), and spatially smoothed with a Gaussian kernel of 5.0 mm full width at half maximum.

The resulting time series was then convolved using a double-gamma function. Only correct trials were used in the analysis. For the first-level analysis, 4D data from each functional run for each participant was analyzed comparing congruent and incongruent trials. The parameter estimate maps and variance maps for the incongruent > congruent contrast were forwarded to a second-level fixed-effects analysis, where all 6 runs for each participant were combined. Any runs showing an excessive amount of head motion (i.e., > 2 mm) based on the first-level analyses were excluded at this point. All runs were given equal weighting in the model.

The third-level analysis was also a fixed-effects analysis where the 2 time points were combined (baseline and trial completion). Contrasts from the second-level analysis were used. The main contrast of interest was longitudinal changes within each participant, specifically trial completion > baseline. This contrast was used in the final mixed effects.

Lastly, the mixed-effects analysis was performed, where data from all participants were combined at the group level. We used FLAME in FSL, in order to accurately model and estimate group differences. Third-level contrasts were used as inputs. Statistically significant clusters of activation were identified on the entire group statistical map by using a voxel-wise threshold to $z > 1.65$ ($p < 0.05$) combined with a cluster probability threshold of $p < 0.05$ (Worsley et al., 1992).

We identified clusters that showed significant change in the incongruent > congruent contrast for trial completion compared with baseline for all participants. In total, 12 regions of interest (ROIs) were identified. Based on the Montreal Neurological Institute (MNI) coordinates of the peak location in each significant cluster, we created spherical ROIs centered on the coordinates, equaling approximately 125 anatomical voxels. Once ROIs were identified, percent signal changes were extracted for each group at each time point separately from the contrast of incongruent > congruent at the second level using Featquery within FSL. The most probable anatomical label for each ROI was determined using the Harvard-Oxford Cortical Structural Atlas packaged in FSL. The percentage signal changes were then imported to SPSS and were analyzed using SPSS (Windows Version 17.0; SPSS Inc., Chicago, IL, USA).

We compared the magnitude of the incongruent minus congruent estimated event-related responses (or percent signal change) of each cortical area between groups by 2 planned simple contrasts: (1) RT1 versus BAT; and (2) RT2 versus BAT. In these contrasts, baseline values were used as a covariate. To reduce the possibility of a type I error, the overall alpha was set at $p < 0.03$.

2.9. Correlation between change in cortical activation and change in flanker task performance

Among those cortical areas that demonstrated a significant between-group difference in percent signal change at trial completion, we assessed the partial correlation, after controlling for experimental group, between change in cortical activation and change in flanker task performance. Change in activation was calculated as percent signal change at trial completion minus percent signal change at baseline. Change in performance was calculated as interference score at baseline minus interference score at trial completion.

3. Results

3.1. Participants

A total of 88 participants were scanned by fMRI at baseline. Seventeen of the 88 participants did not complete scanning at trial completion. An additional 19 participants were excluded because of: (1) left-handedness ($n = 5$); (2) excessive head motion (i.e., > 2 mm) during the baseline scan ($n = 4$) or during the trial completion scan ($n = 2$); (3) data acquisition problems (e.g., warping in data; $n = 5$); or (4) 0% accuracy on their performance of the cognitive-challenging task ($n = 3$). Fifty-two participants were included in our analysis. Specifically, we analyzed fMRI data from 20 participants from the RT1 group, 15 from the RT2 group, and 17 from the BAT group. Baseline demographic and characteristics of the 52 participants who completed both the baseline and the 12-month fMRI scanning are shown in Table 1. There were no significant between-group differences in exercise compliance at trial completion. The RT1 group had an average compliance of 75.1%, 79.2% for the RT2 group, and 71.8% for the BAT group.

3.2. Behavioral results

The RT2 group demonstrated a significant reduction in interference compared with the BAT group ($p < 0.05$), while the RT1 group did not. There was no significant

Table 1
Descriptive statistics for descriptors

Variable	BAT (n = 17), mean (SD)	RT1 (n = 20), mean (SD)	RT2 (n = 15), mean (SD)	Total (n = 52), mean (SD)
Age (y)	69.2 (3.2)	69.7 (2.8)	68.9 (3.2)	69.3 (3.0)
Height (cm)	162.4 (5.9)	161.7 (7.5)	162.7 (6.6)	162.2 (6.6)
Weight (kg)	67.3 (9.5)	70.7 (13.8)	68.7 (10.9)	69.1 (11.6)
Education[a]				
Less than grade 9	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
Grade 9–12 without certificate or diploma	1.0 (5.9)	2.0 (10.0)	0.0 (0)	3.0 (5.8)
High school certificate or diploma	1.0 (5.9)	2.0 (10.0)	3.0 (20.0)	6.0 (11.5)
Trades or professional certificate or diploma	5.0 (29.4)	2.0 (10.0)	2.0 (13.3)	9.0 (17.3)
University certificate or diploma	3.0 (17.6)	5.0 (25.0)	3.0 (20.0)	11.0 (21.2)
University degree	7.0 (41.2)	9.0 (45.0)	7.0 (46.7)	23.0 (44.2)
MMSE score (maximum 30 points)	29.1 (1.1)	28.6 (1.2)	29.1 (0.8)	28.9 (1.1)
Falls in the last 12 months (yes/no)[a]	5 (31.3)	7 (35.0)	5 (33.3)	17 (33.3)
Geriatric Depression Scale (maximum 15 points)	0.0 (0.0)	0.2 (0.9)	0.9 (2.0)	0.3 (1.2)
Functional comorbidity index (maximum 18 points)	1.9 (1.5)	2.2 (2.0)	1.3 (1.2)	1.8 (1.6)
Physical activity scale for the elderly	120.0 (38.4)	115.3 (61.2)	147.2 (68.8)	126.1 (57.8)
Timed Up and Go test (s)	6.4 (1.1)	6.7 (0.8)	6.1 (1.0)	6.4 (1.0)

BAT, twice-weekly balance and tone training; MMSE, Mini Mental State Examination; RT1, once-weekly resistance training; RT2, twice-weekly resistance training.
[a] Count = number of "yes" cases within each group (percent of "yes" within each group).

Table 2
Descriptive statistics for flanker task behavioral data

Variable	BAT (n = 17), mean (SD)	RT1 (n = 20), mean (SD)	RT2 (n = 15), mean (SD)	Total (n = 52), mean (SD)
Baseline				
Congruent trials reaction time (ms)	704.9 (161.3)	640.1 (95.4)	624.4 (85.6)	657.8 (122.4)
Incongruent reaction time (ms)	831.5 (177.2)	762.1 (122.2)	812.3 (122.8)	799.8 (143.8)
Δ Incongruent minus congruent (ms)	139.7 (55.2)	122.0 (60.0)	167.4 (70.0)	140.7 (62.8)
Interference score	18.5 (7.8)	19.1 (8.8)	30.4 (13.7)	22.1 (11.2)
Trial completion				
Congruent trials reaction time (ms)	622.2 (109.9)	565.9 (106.0)	577.3 (93.0)	587.6 (104.7)
Incongruent reaction time (ms)	724.7 (122.2)	661.4 (141.0)	700.1 (110.7)	693.3 (127.3)
Δ Incongruent minus congruent (ms)	97.8 (41.6)	95.5 (51.2)	122.8 (43.1)	104.1 (46.6)
Interference score	17.6 (9.0)	15.3 (7.0)	16.2 (24.3)	16.2 (14.5)

Interference score calculated as {[(incongruent reaction time − congruent reaction time)/congruent reaction time] × 100}.
BAT, twice-weekly balance and tone training; RT1, once-weekly resistance training; RT2, twice-weekly resistance training.

difference between the RT2 group and the RT1 group ($p > 0.05$). Specifically, the RT1 group had a 2.29% reduction in interference at trial completion relative to baseline, the RT2 group had an 8.48% reduction, and the BAT group had a 1.47% reduction. Reduced interference reflects improved performance. There were no significant between-group differences in change in either congruent or incongruent reaction times separately. Table 2 provides the descriptive statistics for the flanker behavioral data.

3.3. fMRI results

Based on the group map for all participants, we identified cortical areas showing significant changes in hemodynamic activity for incongruent versus congruent trials at trial completion relative to baseline. The 12 ROIs are listed and illustrated, respectively, in Table 3 and Fig. 2. No regions showed decreased activity on incongruent versus congruent trials over time.

Between-groups comparisons revealed significantly greater percent signal change in both the left anterior insula extending into lateral orbital frontal cortex and the anterior portion of the left middle temporal gyrus for the RT2 group compared with the BAT group ($p < 0.03$). Figs. 3 and 4 illustrate the percent signal change for each group at each time point for congruent and incongruent trials separately. Fig. 3 highlights that the difference between the BAT group and the RT2 group in the left anterior insula extending into lateral orbital frontal cortex was due to both an increase in activation at trial completion for incongruent trials for the RT2 group and a reduction in activation at trial completion for congruent trials. Fig. 4 highlights that the difference between the BAT group and the RT2 group in the anterior portion of the left middle temporal gyrus was largely due to a reduction in activation at trial completion for congruent trials for the group RT2. There were no differences between the RT1 group and the BAT group ($p > 0.03$).

3.4. Partial correlation results

After controlling for experimental group, change in activation of the left anterior insula extending into lateral

Table 3
Clusters identified as being significantly more active for incongruent trials > congruent trials for the entire group (n = 52) at trial completion compared with baseline

Hemisphere	Region	Cluster size[a]	Max Z[b]	MNI coordinates[c] X	Y	Z
Right	Anterior cingulate gyrus	3432	2.92	2	2	32
Right	Insula		2.88	38	−20	0
Left	Supramarginal gyrus		2.84	−38	−32	36
Right	Angular gyrus/middle temporal gyrus		2.83	56	−48	14
Left	Postcentral gyrus		2.77	−28	−36	56
Left	Supracalcarine cortex	2008	3.29	−22	−66	16
Left	Precuneus		2.89	−18	−60	4
Left	Intracalcarine cortex		2.75	−20	−68	6
Left	Anterior insula/lateral orbital frontal cortex	1215	3.07	−34	14	−16
Left	Anterior middle temporal gyrus		2.88	−62	−8	−12
Left	Temporal pole/superior temporal gyrus		2.71	−60	4	−12
Left	Temporal pole		2.65	−54	16	−22

[a] Cluster size = size of maximum cluster in voxels.
[b] Max Z = the maximum Z statistic for the cluster.
[c] MNI coordinates = location of the cluster maxima in Montreal Neurological Institute standard space.

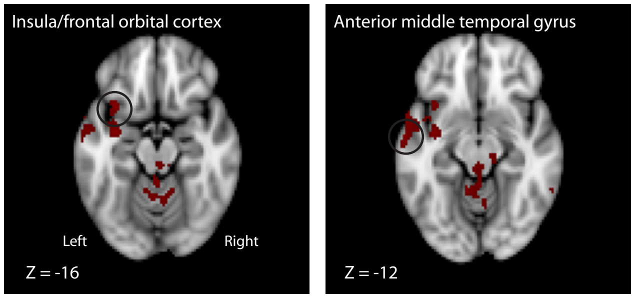

Fig. 2. Cortical recruitment as a function of resistance training. Contrast maps represent increases in activation at trial completion compared with baseline for greater activation in incongruent trials relative to congruent trials. Significantly greater activation was found for twice-weekly resistance training (RT2) compared with twice-weekly balance and tone training (BAT) in the left anterior insula extending into lateral orbital frontal cortex and the anterior portion of the left medial temporal gyrus.

orbital frontal cortex and change in the anterior portion of the left middle temporal gyrus were not significantly associated with change in flanker task performance ($p \geq 0.094$).

4. Discussion

Our findings indicate that senior women who engaged in twice-weekly resistance training significantly improved their performance on the flanker task; this co-occurred with positive functional changes in hemodynamic activity in regions of cortex commonly associated with response inhibition processing in flanker-type tasks—the left anterior insula extending into lateral orbital frontal cortex and the anterior portion of the left middle temporal gyrus (Banich et al., 2000; Boehler et al., 2010; de Zubicaray et al., 2000; Leung et al., 2000). Our data suggest that the performance benefits of resistance training may be functionally mediated, at least in part, by a more efficient engagement of response inhibition processes. Specifically, compared with twice-weekly balance and tone training, the twice-weekly resistance training group demonstrated increased activity in left anterior insula extending into lateral orbital frontal cortex on incongruent trials from baseline to study completion, suggesting an enhanced ability to engage response inhibition processes specifically on these trials. Concurrently, the twice-weekly resistance training group demonstrated reduced activity in both left anterior insula and the anterior portion of the left middle temporal gyrus on congruent trials from baseline to study completion. This suggests that participants of the twice-weekly resistance training group, at baseline, were engaging response inhibition processes regardless of trial type, as if preparing for response conflict as a default state. In contrast, at study completion, participants were more adaptive or demonstrated flexible use of these resources in response to the immediate dictates of the trial type. Taken together, our study thus provides good evidence that resistance training has a positive effect on functional plasticity in cortex. However, we highlight that this effect of resistance training was only observed among those who trained twice weekly; participants of the once-weekly resistance training did not demonstrate comparable response profiles, both in behavioral performance and hemodynamic activity in cortex. Might our study have simply lacked sufficient power to show such an effect in the RT1 group? We highlight that our study is the largest fMRI-based exercise intervention trial to date and doubles the intervention period of the previous randomized control trial using fMRI

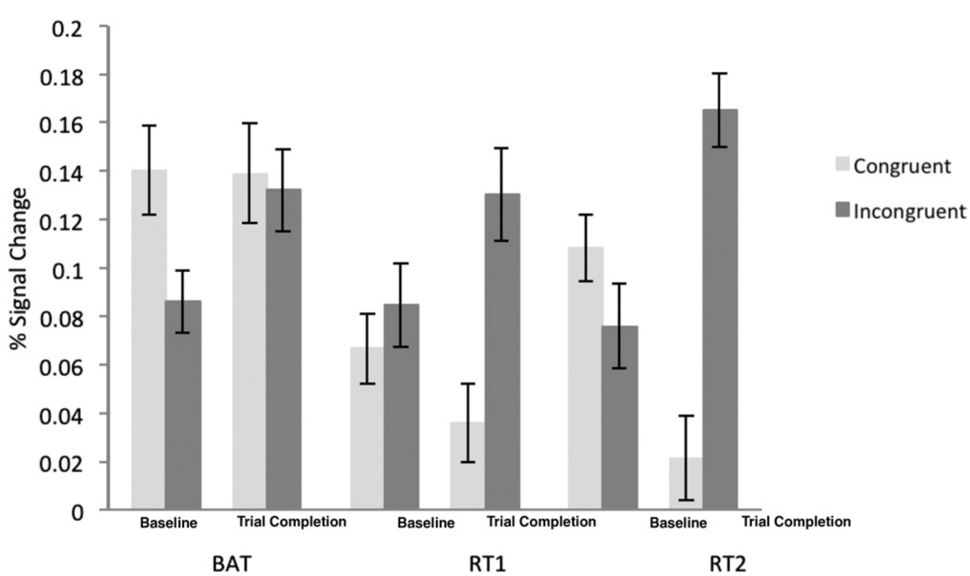

Fig. 3. Percent signal change in the left anterior insula extending into lateral orbital frontal cortex for each group (i.e., twice-weekly balance and tone training [BAT], once-weekly resistance training [RT1], and twice-weekly resistance training [RT2]) as a function of time (i.e., baseline vs. trial completion) and trial type (i.e., congruent vs. incongruent). Error bars represent standard error of the means.

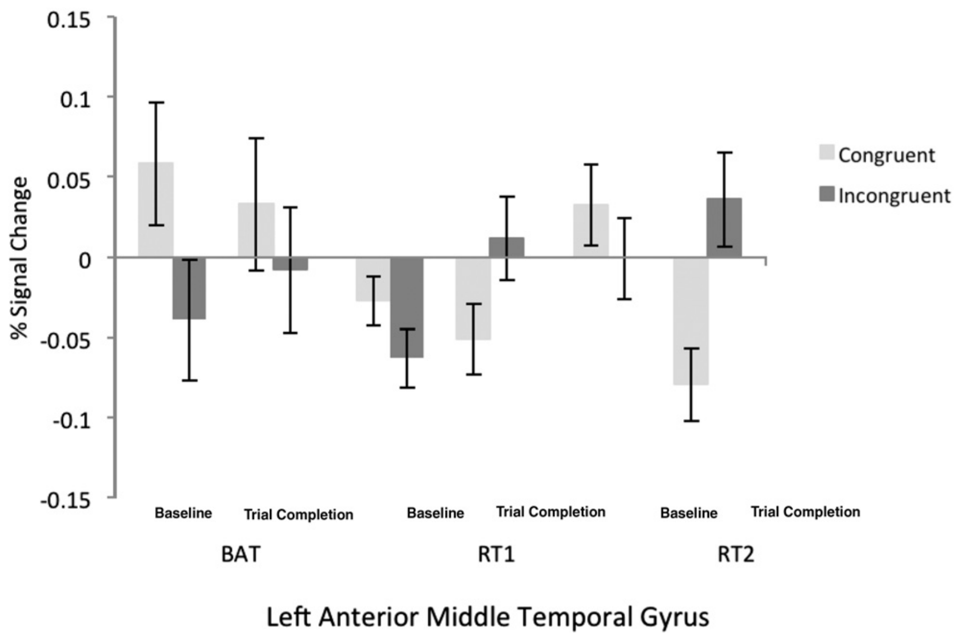

Fig. 4. Percent signal change in the left anterior middle temporal gyrus for each group (i.e., twice-weekly balance and tone training [BAT], once-weekly resistance training [RT1], and twice-weekly resistance training [RT2]) as a function of time (i.e., baseline vs. trial completion) and trial type (i.e., congruent vs. incongruent). Error bars represent standard error of the means.

to investigate the effect of exercise on functional plasticity in seniors (Colcombe et al., 2004).

The results of this study concur and extend the current understanding of the importance of progressive resistance training for maintaining functional independence among older adults (Liu and Latham, 2009). For more than a decade in the USA, resistance training has been recommended for adults, particularly seniors, as a primary prevention intervention, and increasing the prevalence of resistance training is an objective of Healthy People 2010 (United States Department of Health and Human Services, 2010). Resistance training has an established role in reducing morbidity among seniors and provides a broad range of systemic benefits (Borst, 2004; Layne and Nelson, 1999; Skelton et al., 1995; Taaffe et al., 1999; Trappe et al., 2002), including moderating the development of sarcopenia—something that aerobic-based exercise training does not do. The multifactorial deleterious sequelae of sarcopenia include increased falls and fracture risk as well as physical disability. As such, we emphasize that resistance training may be of particular importance to senior women as they are at greater risk for falls and fractures compared with senior men.

How does the positive impact of resistance training on functional plasticity in cortex compare with those of aerobic exercise training? In the only previous comparable randomized control trial (Colcombe et al., 2004), a 6-month aerobic exercise training program increased activity in the frontal and superior parietal regions and decreased activity in the anterior cingulate cortex when participants performed the flanker task. In response inhibition paradigms, increased activity in the superior parietal region has been tied to increased engagement of selective attention processes, whereas decreased activity in the anterior cingulate is associated with a corresponding drop in response conflict monitoring (Banich et al., 2000; de Zubicaray et al., 2000; Leung et al., 2000). This suggests that aerobic exercise training in the previous study (Colcombe et al., 2004) had a positive effect on the ability to selectively attend, or perceptually filter out, task-irrelevant information. In comparison, we found effects of twice-weekly resistance training in a set of cortical regions—the left anterior insula extending into lateral orbital frontal cortex and the anterior portion of the left middle temporal gyrus—that are associated with response inhibition processes, or the ability to avoid making automatic, unwanted responses (Banich et al., 2000; Boehler et al., 2010; de Zubicaray et al., 2000; Leung et al., 2000). Hence, it may be possible to target different subsets of basic cognitive functions in seniors using different exercise strategies—either aerobic or resistance exercise interventions.

What are possible underlying mechanisms whereby resistance training positively impacts functional plasticity? As we highlighted earlier, in humans, resistance training reduced serum homocysteine (Vincent et al., 2003) and increased levels of IGF-1 (Borst et al., 2001; Cassilhas et al., 2007). Increased homocysteine levels are negative cognitive and brain structure outcomes (Den Heijer et al., 2003; Garcia et al., 2004; Sachdev, 2005; Schafer et al., 2005; Seshadri et al., 2002; Vermeer et al., 2002; Wright et al., 2005). IGF-1, in contrast, promotes neuronal growth, survival, and differentiation and improves cognitive performance (Cotman and Berchtold, 2002). Cassilhas and coworkers (2007) demonstrated that 6 months of either moderate- or high-intensity resistance training significantly improved cognitive performance among senior men. They also found serum IGF-1 levels were higher in the resistance training groups than in the control group. Thus, resistance training may promote both cognitive performance and functional plasticity among seniors via mechanisms involving IGF-1 and homocysteine.

Finally, we report several important caveats and limitations. First, our participant sample was limited to generally healthy community-dwelling women aged 65 to 75 years—thus, the findings may not generalize to men or to women of other ages. Second, our study does not address whether 3 or more sessions per week could influence functional plasticity, or whether such training could improve plasticity sooner than 1 year. Finally, because our study did not assess potential biomarkers such as serum homocysteine, we are unable to provide evidence of suggested underlying mechanisms. Last, we recognize that the voxels with the highest peaks in our fMRI analyses may not be the most discriminating between groups. This suggests that our results may be a conservative estimate of the actual effects.

In summary, twice-weekly resistance training in seniors can positively affect functional plasticity of response inhibition processes in cortex. Hence, much like resistance training can improve the muscle tone of the aging body, it also can tone the aging brain.

Disclosure statement

All authors have nothing to declare.

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.

Acknowledgements

The authors thank the Vancouver South Slope YMCA management and members who enthusiastically supported the study by allowing access to participants for the training intervention. The authors are indebted to Ms. Lindsay Katarynych for coordinating this study. We thank the instructors for their commitment to the participants' health and safety.

The Vancouver Foundation (BCMSF, Operating Grant to TLA), Natural Sciences and Engineering Research Council of Canada (NSERC, Operating Grant to TCH), and the Michael Smith Foundation for Health Research (MSFHR, Establishment Grant to TLA) provided funding for this study. The Canada Foundation for Innovation funded essential infrastructure used in this study (New Opportunities Fund to TLA). Drs. Liu-Ambrose and Handy are MSFHR Scholars. Dr. Liu-Ambrose is also a Canadian Institute of Health Research New Investigator. Ms. Nagamatsu is a MSFHR and NSERC Ph.D. trainee.

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