Four weeks of combination exercise training improved executive functions, episodic memory, and processing speed in healthy elderly people: evidence from a randomized controlled trial

Rui Nouchi · Yasuyuki Taki · Hikaru Takeuchi · Atsushi Sekiguchi · Hiroshi Hashizume · Takayuki Nozawa · Haruka Nouchi · Ryuta Kawashima

Received: 22 May 2013 / Accepted: 16 September 2013 / Published online: 25 September 2013
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Abstract Previous reports have described that long-term combination exercise training improves cognitive functions in healthy elderly people. This study investigates the effects of 4 weeks of short-term combination exercise training on various cognitive functions of elderly

Electronic supplementary material The online version of this article (doi:10.1007/s11357-013-9588-x) contains supplementary material, which is available to authorized users.

R. Nouchi (✉)
Human and Social Response Research Division,
International Research Institute of Disaster Science,
Tohoku University,
4-1 Seiryochō, Aobaku, Sendai 980-8575, Japan
e-mail: rnouchi@idac.tohoku.ac.jp

R. Nouchi · T. Nozawa · H. Nouchi · R. Kawashima
Smart Ageing International Research Centre, Institute of
Development, Aging and Cancer, Tohoku University,
Sendai 980-8575, Japan

Y. Taki · A. Sekiguchi
Division of Medical Neuroimage Analysis, Department of
Community Medical Supports, Tohoku Medical Megabank
Organization, Tohoku University,
4-1 Seiryō-machi, Sendai 980-8575, Japan

Y. Taki · H. Takeuchi · H. Hashizume · R. Kawashima
Division of Developmental Cognitive Neuroscience,
Institute of Development, Aging and Cancer,
Tohoku University,
Sendai 980-8575, Japan

A. Sekiguchi · R. Kawashima
Department of Functional Brain Imaging, Institute of
Development, Aging and Cancer, Tohoku University,
Sendai 980-8575, Japan

people. We conducted a single-blinded randomized controlled trial with two parallel groups. Sixty-four healthy older adults were assigned randomly to a combination exercise training group or a waiting list control group. Participants in the combination exercise training group participated in the combination exercise training (aerobic, strength, and stretching exercise trainings) 3 days per week during 4 weeks (12 workouts total). The waiting list control group did not participate in the combination exercise training. Measures of the cognitive functions (executive functions, episodic memory, working memory, reading ability, attention, and processing speed) were conducted before and after training. Results showed that the combination exercise training improved executive functions, episodic memory, and processing speed compared to those attributes of the waiting list control group. This report was the first of a study demonstrating the beneficial effects of short-term combination exercise training on diverse cognitive functions of elderly people. Our study provides important evidence of the short-term combination exercise's effectiveness.

Keywords Combination exercise training · Cognitive plasticity · Intervention · Cognitive function

Background

Cognitive functions decline with age. For instance, elderly people might experience a decline in several cognitive functions such as memory, attention (Yakhno et al. 2007), executive functions (Royall et al. 2004),

and processing speed (Salthouse 1996). Degraded in cognitive ability engenders difficulty in performing basic daily living activities (Cahn-Weiner et al. 2000; Owsley and McGwin 2004). Consequently, maintaining or improving cognitive function in older adults is drawing increasing attention (Colcombe and Kramer 2003).

Previous studies have demonstrated that combination exercise training, which combines exercise training of different types (e.g., aerobic and strength exercise training), can also facilitate improvement of cognitive functions (Snowden et al. 2011; Smith et al. 2010; Tseng et al. 2011). For example, a randomized controlled trial (RCT) study showed that combination exercise training for 42 weeks improved processing speed and memory (Williams and Lord 1997). Moreover, a meta-analysis showed that combination training has a greater effect than aerobic exercise training alone (Colcombe and Kramer 2003). Combination exercise training appears to be the most effective exercise training for improving cognitive function.

Although earlier studies showed that long-term (>24 weeks) combination exercise training can improve memory functions in elderly people (Colcombe and Kramer 2003; Snowden et al. 2011; Smith et al. 2010; Tseng et al. 2011; Williams and Lord 1997), an unresolved issue remains. It remains unclear whether short-term combination exercise training can improve diverse cognitive functions (e.g., executive functions and attention) or not in healthy elderly people. This study was conducted to ascertain whether 4 weeks of combination exercise training can improve diverse cognitive functions or not in healthy elderly people. To reveal the beneficial effects of combination exercise training on widely various cognitive functions, we conducted a single-blinded RCT. Testers were blinded to the study hypothesis and the group membership of participants. We assessed a broad range of cognitive functions. The measured cognitive functions were divisible into seven categories: executive functions, episodic memory, working memory, reading ability, attention, and processing speed.

Based on previous studies using combination exercise training, we hypothesized that the short-term exercise training improves executive functions, episodic memory, and processing speed. First, short-term intervention (4 weeks) using cognitive intervention led to improve executive function and processing speed in healthy elderly (Nouchi et al. 2012a). A second reason was that a

previous study demonstrated combination exercise training improvements of episodic memory and processing speed (Williams and Lord 1997). Finally, earlier studies using aerobic exercise training alone or using strength exercise training alone showed improvements of executive functions (Colcombe and Kramer 2003; Smith et al. 2010; Tseng et al. 2011). The combination exercise training used in this study included aerobic and strength exercise training (see “Method”). Therefore, we assumed that combination exercise training improves executive functions.

Method

Randomized controlled trial design and setting of this trial

This study, which was registered in the University Hospital Medical Information Network (UMIN) Clinical Trial Registry (UMIN000007828), was an RCT conducted in Sendai City, Miyagi Prefecture, Japan. The study protocol was described in a previous report (Nouchi et al. 2012b). Written informed consent to participate in the study was obtained from each participant before enrollment. The study protocol was approved by the Ethics Committee of the Tohoku University Graduate School of Medicine. Informed consent was obtained from all participants.

To assess the impact of short-term combination exercise on diverse cognitive functions in healthy elderly people, we used a single-blinded intervention with two parallel groups: a combination exercise training group and a waiting list control group. Testers were blind to the study's hypothesis and to the group membership of participants. The Consolidated Standards of Reporting Trials (CONSORT) statement (<http://www.consort-statement.org/home/>) was used as a framework for developing the study methodology (see [Supplementary materials](#)). The trial design is presented in Fig. 1.

Inclusion and exclusion criteria

The purpose of this intervention was to investigate the beneficial effects of combination exercise training on diverse cognitive functions in healthy older adults. Criteria included participants who reported themselves as right-handed, native Japanese speakers, unconcerned about their own memory functions, not using

Fig. 1 CONSORT flowchart

medications known to interfere with cognitive functions (including benzodiazepines, antidepressants, and other central nervous agents), and having no disease known to affect the central nervous system, including thyroid disease, multiple sclerosis, Parkinson disease, stroke, severe hypertension (systolic blood pressure over 180, diastolic blood pressure over 110), and diabetes. The age of participants was 60 years old or older. After eliciting the information above using a semistructured telephone interview and self-report questionnaire, we

met prospective participants and checked their blood pressure at the start of this study.

Criteria excluded participants who had an intelligence quotient (IQ) of less than 85 derived from the Japanese Reading Test (JART) (Matsuoka et al. 2006), a score of Mini Mental Status Exam (MMSE) less than 26 (Folstein et al. 1975), or a score of Frontal Assessment Battery at bedside (FAB) less than 12 (Dubois et al. 2000). MMSE (Folstein et al. 1975), a 20-item instrument, is the most widely used screening instrument for

the detection of cognitive impairment in older adults. The MMSE items measured orientation for place and time, memory and attention, language skills, and visuospatial abilities. MMSE was scored from 0 to 30, with lower scores indicating greater degrees of general cognitive dysfunction. FAB (Dubois et al. 2000) evaluated executive functions. FAB consisted of six subtests, namely, those for similarities (conceptualization), lexical fluency (mental flexibility), motor series (programming), conflicting instructions (sensitivity to interference), go–no go (inhibitory control), and prehension behavior (environmental autonomy). FAB was scored from 0 to 18. Lower scores of FAB indicated greater degrees of executive dysfunction. This criterion was the same as that used in our previous study, which investigated the beneficial effects of cognitive training using video games during 4 weeks (Nouchi et al. 2012a). Participants who were participating in another cognitive-related intervention studies while joining this intervention were excluded. For the current study, we also recruited participants who (1) were not participating in another exercise studies, (2) did not exercise regularly, and (3) were not members of a gym or a health club. Consequently, participants already exercising were excluded. No participants were engaged in any exercise program at the starting point of the intervention.

Participants

Eighty-one participants were recruited from the general population through advertisements in the local town paper and local newspaper (Fig. 1). Interested participants were screened using a semistructured telephone interview. After the telephone interview, four people were excluded because they were taking medications known to interfere with cognitive functions (including benzodiazepines, antidepressants, and other central nervous agents); another six people were excluded based on severe hypertension (systolic blood pressure over 180, diastolic blood pressure over 110) and diabetes. Seven participants declined to participate before a random assignment. All participants ($n=64$) were invited to visit Tohoku University for a more detailed screening assessment (MMSE (Folstein et al. 1975) and FAB (Dubois et al. 2000)) and to provide written informed consent. No participant was excluded on MMSE and FAB scores. Table 1 presents the baseline demographics and neuropsychological characteristics of the participants included in these analyses.

Table 1 Characteristics of participants in the combination exercise training and the waiting list control groups

	Combination exercise group		Waiting list control group		<i>p</i> value
	Mean	SD	Mean	SD	
Age (years)	66.75	(4.61)	67.06	(2.82)	0.75
Education (years)	13.44	(1.85)	13.19	(1.96)	0.60
MMSE (score)	27.91	(1.25)	27.94	(1.27)	0.92
FAB (score)	14.25	(1.52)	14.28	(1.51)	0.93

No significant difference was found between combination exercise training and the waiting list control groups (two sample *t* test, $p>0.10$)

MMSE Mini Mental State Examination, FAB Frontal Assessment Battery at bedside, SD standard deviation

Sample size

Our sample size estimation was based on the change score in the reverse Stroop task, which was the primary outcome in this study. The primary outcome measure was the Stroop test (ST), which we selected because (1) previous studies using exercise training showed that exercise training can improve executive functions (Anderson-Hanley et al. 2010), (2) ST was a task that is often used to measure executive functions (Alvarez and Emory 2006), and (3) ST has been standardized, with high reliability and validity in Japanese populations (Hakoda and Sasaki 1990).

This study uses eta-squared (η^2) as an index of effect size. As a descriptive index of strength of association between an experimental factor (main effect or interaction effect) and a dependent variable, η^2 is defined as the proportion of total variation attributable to the factor. It ranges in value from 0 to 1 (Cohen 1988). Using information (sums of squares for total, SS total; the sum of squares for factor, SS factor) reported in an analysis of covariance (ANCOVA) summary table, we calculated η^2 (SS factor divided by SS total). SS factor was the variation attributable to the factor and SS total was the total variation which includes the SS factor and the sum of squares for error. In actuality, $\eta^2 \geq 0.01$ was regarded as a small effect, $\eta^2 \geq 0.06$ as a medium effect, and $\eta^2 \geq 0.14$ as a large effect (Cohen 1988). We expected to detect a large effect size ($\eta^2=0.14$) of the change score (posttraining score minus pretraining score) in the reverse Stroop task between combination exercise and waiting list groups. The sample size was

determined using G*Power (Faul et al. 2007, 2009) based on 80 % power, a two-sided hypothesis test, an alpha level of 5 %, an ANCOVA model that includes a baseline reverse Stroop task score, age and sex as a covariate. The sample size calculation indicated the need for 32 participants in each of the combination exercise and waiting list groups with consideration of a 20 % drop-out rate.

Randomization

Randomization was designed to take place after receiving informed consent statements. A researcher (R. N.) who had no contact with the study participants assigned the participants to either the combination exercise group or the waiting list control group using a random allocation sequence. The random allocation sequence was generated using a spreadsheet program (Excel 2003; Microsoft Corp.) with the function (RAND) with no blocks or restrictions. Letters were used to inform participants of their group allocation.

Intervention group (combination exercise training group)

The intervention group received the following combination exercise training developed by Curves (Curves Japan Co., Ltd.). The combination exercise combined training of three types: aerobic, strength, and stretching (<http://www.curves.co.jp/consistency/program/>). Participants performed the combination exercise training 3 days per week throughout the 4 weeks (12 workouts total). For several reasons, we selected a 4-week length of intervention. First, a previous study showed that cognitive functions in the older adults improved after 4 weeks of intervention using cognitive intervention (Nouchi et al. 2012a). Second, a meta-analysis study revealed that the effect size of short-term duration exercise training (4–12 weeks) was greater than that of medium duration exercise training (from 16 to 24 weeks) (Colcombe and Kramer 2003). Based on these reasons, we selected 4 weeks of intervention duration.

Each circuit-style workout consists of 12 strength training exercise (chest press/seated row, squat, shoulder press/lat pull, leg extension/leg curl, abdominal crunch/back extension, lateral lift, elbow flexion/extension, horizontal leg press, pectoral deck, oblique, hip abductor/adductor, gluteus; <http://www.curves.co.jp/consistency/program/point01/>). The strength

training machines included calibrated pneumatic resistance pistons that allowed for opposing muscle groups to be trained in a concentric-only fashion. Participants were informed of the proper use of all equipment and were instructed to complete as many repetitions in a 30-s time period. In a continuous interval fashion, participants performed floor-based aerobic training (e.g., running/skipping in place and arm circles) on recovery pads for a 30-s time period after each resistance exercise in an effort to maintain a consistent exercise heart rate corresponding to 60–80 % of their heart maximum heart rate. All workouts were supervised by trained exercise instructors who assisted with proper exercise technique and maintenance of adequate exercise intensity. Participants must complete two circuits (24 min). After two rotations, participants did standardized whole-body stretching training (6 min). The whole-body stretching training consists of 12 stretching exercise (Achilles' tendon, sole of the foot, thigh, armpit, shoulder, shoulder/upper arm, chest/arm, shoulder/chest/arm, waist, back of knee, base of thigh, back; <http://www.curves.co.jp/consistency/program/point02/>).

Waiting list control group (no combination exercise training group)

The waiting list control group received no intervention. Those participants were informed by letter that they were scheduled to receive an invitation to participate after a waiting period of 4 weeks. We asked the waiting list control group not to go to the gym and not to join an exercise program during the waiting period. This study used no active control group such as a stretch exercise training group alone or a placebo group such as a social contact group, because results of previous intervention showed no difference in cognitive or functional improvement between the stretch exercise training group (active control group) and non-exercise control group (control group) (Brown et al. 2009) or between the social-contact group (placebo group) and no-social-contact group (control group) (Mahncke et al. 2006; Clark et al. 1997). Moreover, using the waiting list control group had the advantage of letting everyone in the study receive the new intervention such as the combination exercise training (sooner or later). Therefore, we used the waiting list control group in this intervention study.

Overview of cognitive function measures

To evaluate the beneficial effects of combination exercise on cognitive functions, we assessed a broad range of cognitive functions (Table 2). Measures of the cognitive functions were divisible into six categories (executive functions, episodic memory, working memory, reading ability, attention, and processing speed). Executive functions were measured using ST (Hakoda and Sasaki 1990) and verbal fluency task (VFT) (Ito et al. 2004). Episodic memory was measured using logical memory (LM) (Wechsler 1987) and first and second names (FS-N) (Wilson et al. 1985). Working memory was measured using digit span forward (DS-F) and digit span backward (DS-B) (Wechsler 1997). Reading ability was measured using the Japanese Reading Test (JART) (Matsuoka et al. 2006). Attention was measured using the digit cancellation task (D-CAT) (Hatta et al. 2000). Processing speed was measured using digit symbol coding (Cd) (Wechsler 1997) and symbol search (SS) (Wechsler 1997). Details of all tasks are described in [Supplementary materials](#). We assessed these cognitive function measures before and after the intervention period (4 weeks).

Psychological questionnaire

To evaluate the beneficial effects of combination exercise on quality of life (QOL) for participants, we used questionnaires. To evaluate QOL, we used the Japanese version of WHOQOL-BREF (QOL-26) (Tazaki and Nakane 1997). The QOL-26, a short version of the WHOQOL, was a self-rating instrument that assessed individuals' perceptions of their position in life in the

context of the culture and value system in which they lived and in relation to their goals, expectations, standards, and concerns. The QOL-26 had 26 items with five subscales: Physical (physical state), Psychological (cognitive and affective state), Social (interpersonal relationships and social roles in life), Environmental (relationships to salient features of the environment), and Global (meaning in life, or overarching personal beliefs). A five-point response category was used, ranging from 1, which indicates “strongly disagree,” to 5, which indicates “strongly agree.” The total average score is the average of all 26 items. A higher score denotes better QOL.

For the combination exercise training group only, we asked participants to answer the questionnaires related to the subjective feelings (1 motivation of continuing the combination exercise during the intervention period, 2 fatigue during the intervention period, 3 satisfaction of the intervention during the intervention period, 4 enjoyment of the combination exercise during the intervention period) after the intervention period. Participants rated these questionnaires using a nine-point scale (for the motivation scale, from 1 = very low to 9 = very high; for the fatigue scale, from 1 = very low to 9 = very high; for the satisfaction scale, from 1 = very low to 9 = very high; for enjoyment scale, from 1 = very low to 9 = very high). These questionnaires were used to assess the relation between the change score of cognitive functions after the combination exercise training and the subjective feelings.

Anthropometric measurements

We collected anthropometric measurements (e.g., height, weight, waist circumference, and hip circumference) for the combination exercise training group only. Details of the anthropometric measurements, analysis, and results are presented in [Supplementary materials](#).

Analysis

This study was designed to evaluate the beneficial effects of the short-term combination exercise in elderly people. We calculated the change score (posttraining score minus pretraining score) in all cognitive function measures and then conducted an ANCOVA for the change scores in each cognitive test. The change scores were used as dependent variables. Groups (combination exercise, waiting list control) were used as independent

Table 2 Summary of cognitive function measures

Cognitive function	Task
Executive functions	Stroop test
	Verbal fluency task
Episodic memory	Logical memory
	First and second names
Working memory	Digit span forward
	Digit span backward
Reading ability	Japanese reading test
Attention	Digit cancellation task
Processing speed	Digit symbol coding
	Symbol search

variables. Pretraining scores in the dependent variable, sex, age, the score of MMSE, and the score of FAB were covariates used to adjust for background characteristics and to exclude the possibility that any pre-existing difference of measure between groups affected the result of each measure.

We also calculated the change score (posttraining score minus pretraining score) in the QOL-26. We conducted an ANCOVA for the change scores in the QOL-26. The change score was the dependent variable. Groups (combination exercise, waiting list) were the independent variable. Pretraining scores in QOL-26, sex, age, the score of MMSE, and the score of FAB were covariates to adjust for background characteristics and to exclude the possibility that any pre-existing difference of measure between groups affected the result of each measure.

To assess the relation between the improvements of cognitive functions after the exercise training and the subjective feeling, we also conducted a Pearson's correlation analyses between the change scores in each cognitive test and subjective feelings (e.g., motivation).

The level of significance was set as $p < 0.05$. We used Storey's false discovery rate (FDR) correction methods to adjust the p values (Storey 2002). This study reported η^2 as an index of effect size (please see details in [Supplementary material](#)). Additionally, Cohen's d was used because of its ease in comparison of the beneficial effects of interventions with those reported from other studies.

Missing data were imputed using missing value analysis in the Statistical Package for the Social Sciences (SPSS). Particularly, we imputed missing values using maximum likelihood estimation (Dempster et al. 1977) based on the expectation–maximization algorithm with the observed data in an iterative process (Dempster et al. 1977). All randomized participants were included in the analyses in line with their allocation, irrespective of how many sessions they completed (intention-to-treat principle). All analyses were performed using software (SPSS, ver. 18 or higher; SPSS Japan Inc.).

Results

As presented in Fig. 1, the 64 participants in this study were randomized into two groups (combination exercise training and waiting list control). The study was completed by 30 of the 32 members in the combination

exercise training group and 31 of the 32 members in the waiting list control group. Table 1 presents the baseline demographics and neuropsychological characteristics of the participants. Based on the intention-to-treat principle, we imputed missing values of two participants in the combination exercise training group and a participant in the waiting list control group (see “[Analysis](#)”). The pretraining and posttraining scores in cognitive functions are presented in Table 3.

To evaluate the beneficial effect of the short-term combination exercise training on the improvement of various cognitive functions, we conducted ANCOVA for the change scores in each of the cognitive tests (Table 4). Results showed that the combination exercise training group improved in all measures of the executive functions (ST, rST, LFT, and CFT), one of two measures of the episodic memory (LM), and all measures of the processing speed (Cd and SS) compared to the waiting list control group. However, the combination exercise training did not improve other cognitive function measures. Statistical values and effect sizes are presented in Table 4. These results demonstrate that the effect of the combination exercise training led to improvements of the executive functions, episodic memory, and processing speed.

To evaluate the beneficial effect of the combination exercise training on the improvement of QOL, we conducted ANCOVA for the change scores in the QOL-26 (pre- and postscores in the combination exercise training group, pre-mean=3.40, SD=0.85, post-mean=3.87, SD=0.88; pre- and postscores in the waiting list control group, pre-mean=3.57, SD=0.81, post-mean=3.90, SD=0.78; change score in the combination exercise training group, mean=0.48, SD=1.07; change score in the wait list control; mean=0.35, SD=0.83). Results showed that the combination exercise training did not improve mental health (QOL-26, $F(1, 57)=0.01$, $\eta^2=0.00$). To investigate the relations between the improvements of cognitive functions and the subjective feelings, we conducted Pearson's correlation analyses for scores of the combination exercise training group. Results showed no significant correlation between the improvement of cognitive functions and the subjective feelings (Table 5).

Discussion

This study was designed to investigate the beneficial effects of short-term combination exercise training on

Table 3 Cognitive function scores before and after training periods in both groups

	Combination exercise group				Waiting list control group				Effect size (<i>d</i>) ^a	<i>p</i> value ^a
	Pre		Post		Pre		Post			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
Executive functions										
LFT (number)	9.10	(2.60)	10.58	(2.17)	8.90	(2.48)	9.60	(2.07)	0.08	0.760
CFT (number)	12.40	(3.88)	15.27	(2.38)	12.77	(3.04)	13.38	(2.55)	0.11	0.671
rST (number)	45.33	(7.27)	51.57	(6.50)	46.61	(6.65)	49.16	(7.01)	0.18	0.462
ST (number)	31.40	(4.93)	35.88	(5.49)	30.94	(5.70)	33.42	(6.64)	0.09	0.730
Episodic memory										
LM (score)	8.87	(3.38)	13.54	(2.77)	8.55	(3.85)	11.10	(3.22)	0.09	0.723
FSN (score)	3.54	(2.24)	4.90	(1.97)	3.45	(2.43)	5.26	(1.87)	0.04	0.886
Working memory										
DS-F (score)	5.73	(1.24)	5.93	(1.19)	5.45	(1.16)	5.71	(1.02)	0.23	0.354
DS-B (score)	4.13	(1.36)	4.60	(1.58)	4.16	(0.88)	4.71	(1.51)	0.02	0.924
Attention										
D-CAT (number)	27.83	(6.06)	29.37	(5.68)	26.97	(6.60)	29.61	(5.53)	0.14	0.587
Processing speed										
Cd (number)	69.60	(12.74)	77.46	(13.93)	72.61	(13.95)	76.05	(12.86)	0.23	0.370
SS (number)	34.51	(5.28)	38.55	(4.96)	35.74	(7.24)	37.36	(6.58)	0.20	0.438
Reading ability										
JART (score)	20.43	(3.56)	20.89	(3.59)	19.87	(3.91)	20.61	(3.80)	0.15	0.553

From group comparison (two sample t tests) of the pretraining scores, no significant difference was found in any measure of cognitive functions between the combination exercise group and the waiting list control group ($p>0.10$). Effect size estimates were calculated using Cohen's d : $d=0.20$ is regarded as small effect; $d=0.50$ is medium effect; and $d=0.80$ is a large effect. Executive functions were measured using the Stroop test (ST) and verbal fluency task (VFT). Episodic memory was measured using logical memory (LM) and first and second names (FS-N). Working memory was measured using digit span forward (DS-F) and digit span backward (DS-B). Attention was measured using the digit cancellation task (D-CAT). Processing speed was measured using digit symbol coding (Cd) and symbol search (SS). Reading ability was measured using the Japanese Reading Test (JART)

pre pretraining, *post* posttraining, *SD* standard deviation

^a The effect size and p values refer to baseline differences between the groups

diverse cognitive functions among healthy older adults. The results demonstrated that the short-term combination exercise training led to improve executive functions, episodic memory, and processing speed compared to the non-intervention groups. These results clearly supported our hypothesis.

The present findings are consistent with previously reported evidence which showed that aerobic exercise training and strength training can contribute to the improvements of executive functions, episodic memory, and processing in healthy elderly people (Colcombe and Kramer 2003; Snowden et al. 2011). Additionally, previous studies using combination exercise training demonstrated the improvement of memory performance

after the intervention period (Williams and Lord 1997; Lautenschlager et al. 2008). Nevertheless, this study is the first demonstrating the improvement of executive function, episodic memory, and processing speed after the short-term combination exercise training.

Many reports have described improvements of cognitive function after exercise. In this study, we examined the mechanism of improvement of cognitive functions from a cognitive science perspective and a neuroscience perspective.

From a cognitive science perspective, the present results are explainable using the overlapping hypothesis (Jones et al. 2006; Nouchi et al. 2012a, 2013). The overlapping hypothesis assumes that improvements of

Table 4 Change scores in cognitive function measures of both groups

	Combination exercise		Waiting list control		Effect size (η^2)	Effect size (d)	p value	Adjusted p value	Results of ANCOVA
	Mean	SD	Mean	SD					
Executive functions									
LFT (number)	1.48	(1.62)	0.70	(1.82)	0.06	0.50	0.021	0.023	CE > WL
CFT (number)	2.87	(2.78)	0.61	(2.12)	0.14	0.82	0.000	0.000	CE > WL
rST (number)	6.25	(2.80)	2.55	(3.87)	0.21	1.03	0.000	0.000	CE > WL
ST (number)	4.48	(2.90)	2.48	(3.30)	0.10	0.66	0.013	0.017	CE > WL
Episodic memory									
LM (score)	4.67	(1.96)	2.55	(2.51)	0.20	1.01	0.000	0.000	CE > WL
FSN (score)	1.36	(2.18)	1.81	(2.05)	0.01	0.19	0.355	0.355	n.s.
Working memory									
DS-F (score)	0.20	(1.06)	0.26	(0.98)	0.00	0.06	0.792	0.528	n.s.
DS-B (score)	0.47	(1.16)	0.55	(1.21)	0.00	0.09	0.730	0.531	n.s.
Attention									
D-CAT (number)	1.53	(3.00)	2.65	(6.60)	0.01	0.14	0.512	0.455	n.s.
Processing speed									
Cd (number)	7.86	(3.90)	3.43	(4.76)	0.19	0.97	0.000	0.000	CE > WL
SS (number)	4.04	(2.24)	1.62	(3.43)	0.13	0.77	0.001	0.002	CE > WL
Verbal ability									
JART (score)	0.46	(1.36)	0.74	(1.59)	0.01	0.15	0.551	0.441	n.s.

Change scores were calculated by subtracting the precognitive measure score from the postcognitive measure score. We conducted an analysis of covariance (ANCOVA) for the change scores in each cognitive test. In ANCOVA, pretraining scores in each cognitive test, sex, age score in MMSE, and score in FAB were the covariates. Significance was inferred for $p < 0.05$. The p values were adjusted using FDR method. Moreover, this report describes eta-squared (η^2) as an index of effect size. As a descriptive index of strength of association between an experimental factor (main effect or interaction effect) and a dependent variable, η^2 is defined as the proportion of total variation attributable to the factor: it ranges in value from 0 to 1: $\eta^2 \geq 0.01$ is regarded as a small effect; $\eta^2 \geq 0.06$ is a medium effect; and $\eta^2 \geq 0.14$ is a large effect. We also report Cohen's d as an index of effect size. Cohen's d : $d = 0.20$ is regarded as small effect; $d = 0.50$ is medium effect; and $d = 0.80$ is a large effect. Executive functions were measured using the Stroop test (ST) and verbal fluency task (VFT). Episodic memory was measured using logical memory (LM) and first and second names (FS-N). Working memory was measured using digit span forward (DS-F) and digit span backward (DS-B). Attention was measured using the digit cancellation task (D-CAT). Processing speed was measured using digit symbol coding (Cd) and symbol search (SS). Reading ability was measured using the Japanese Reading Test (JART)

SD standard deviation, n.s. not significant

cognitive functions by a certain type of training (e.g., exercise training or cognitive training) would occur if the processes during both training tasks (e.g., combination exercise training) and untrained tasks (e.g., measures of cognitive functions) are overlapped and are involved in similar cognitive processes. In this study, participants were required to do the combination exercise training, which included aerobic, strength, and stretching exercises. To perform these exercises, executive functions, episodic memory, and processing speed were recruited. For example, executive functions and processing speed are necessary to switch from one exercise to another exercise as quickly as possible, to

conduct the aerobic and strength exercises alternately at the fixed tempo (30 s), to plan complex motor movements during the aerobic exercise, and to complete some actions with as many repetitions as possible during the strength exercise. Moreover, episodic memory is expected to be necessary to master a sequence of actions in the aerobic and stretching exercises and learn the necessary procedures to use the strength machines of 12 types.

Based on the overlapping hypothesis, the improvements of executive functions, episodic memory, and processing speed after the combination exercise training are explainable as follows. First, it would take the

Table 5 Correlations between improvement of cognitive functions and the subjective feelings

	Motivation		Fatigue		Satisfaction		Enjoyment	
	<i>r</i>	<i>p</i> value	<i>r</i>	<i>p</i> value	<i>r</i>	<i>p</i> value	<i>r</i>	<i>p</i> value
Executive functions								
LFT (number)	0.08	0.67	0.03	0.85	−0.01	0.97	−0.19	0.29
CFT (number)	−0.12	0.52	0.22	0.22	−0.29	0.10	0.01	0.94
rST (number)	−0.05	0.78	0.04	0.82	0.22	0.22	−0.07	0.72
ST (number)	0.18	0.32	0.08	0.66	−0.20	0.27	−0.16	0.39
Episodic memory								
LM (score)	−0.06	0.75	0.24	0.19	0.04	0.83	0.05	0.79
FSN (score)	0.11	0.55	0.12	0.51	−0.24	0.18	0.06	0.73
Working memory								
DS-F (score)	−0.01	0.96	−0.15	0.41	−0.02	0.90	−0.12	0.50
DS-B (score)	−0.01	0.98	−0.22	0.22	0.13	0.48	0.03	0.87
Attention								
D-CAT (number)	−0.14	0.44	0.04	0.81	0.04	0.83	0.18	0.31
Processing speed								
Cd (number)	−0.04	0.83	0.04	0.81	−0.18	0.32	0.14	0.44
SS (number)	0.08	0.65	0.14	0.45	−0.20	0.26	0.23	0.20
Reading ability								
JART (score)	−0.07	0.69	0.14	0.46	−0.01	0.95	0.17	0.35

No significant correlation was found between the change score in cognitive functions and the subjective feelings. Change scores were calculated by subtracting the precognitive measure score from the postcognitive measure score. Executive functions were measured using the Stroop test (ST) and verbal fluency task (VFT). Episodic memory was measured using logical memory (LM) and first and second names (FS-N). Working memory was measured using digit span forward (DS-F) and digit span backward (DS-B). Attention was measured using the digit cancellation task (D-CAT). Processing speed was measured using digit symbol coding (Cd) and symbol search (SS). Reading ability was measured using the Japanese Reading Test (JART)

cognitive processes described above to do the combination exercise training. Second, both the combination exercise training and the psychological measures which assessed the cognitive functions might share the same cognitive processes. Third, the cognitive processes described above were enhanced by the combination exercise training. Consequently, executive functions, episodic memory, and processing speed improved during the combination exercise training. From a statistical perspective, this hypothesis may be tested to conduct moderator or mediator analyses using improvements of cognitive processes or performance during the combination exercise training as a moderator or mediator value. In this study, we did not measure cognitive processes or performance during the combination exercise training. In the future, more research should be conducted to measure cognitive processes or performance during the combination exercise training and to conduct moderator or mediator analyses using these measures.

From a neuroscience perspective, improvement of cognitive functions after the combination exercise training can be explained by changes of the brain structure, brain function, and brain connectivity, which are often called the brain plasticity (neural plasticity). Animal studies reported that some molecules such as brain-derived neurotrophic factor (BDNF), insulin-like growth factor (IGF-1), and vascular endothelial growth factor (VEGF) have a central role in brain plasticity, including neurogenesis, angiogenesis, and synaptic plasticity (Monteggia et al. 2004; Neeper et al. 1995; Ding et al. 2006; Chen et al. 2005). Previous studies demonstrated that exercise increased the BDNF, IGF-1, and VEGF levels (Cotman and Berchtold 2002; Fabel et al. 2003; Ding et al. 2004). Consequently, changes of the brain structure, brain function, and brain connectivity can be changed by neurogenesis and angiogenesis (Zatorre et al. 2012). In fact, some previous human neuroimaging studies have revealed brain plasticity after

exercise training. Previous studies using magnetic resonance imaging (MRI) have shown that a certain type of exercise training selectively changes the brain structure, brain function, and brain connectivity in the older adults. For example, one RCT study using MRI showed the increase of the brain volume in the hippocampus, which has an important role in memory functions, after walking exercise training for 1 year (Erickson et al. 2011). Additionally, one functional MRI study demonstrated greater activity in the middle frontal gyrus, which is associated with performance of executive functions and processing speed, during executive function task after aerobic exercise training for 6 months (Colcombe et al. 2004). Moreover, a recent study using resting state fMRI (Voss et al. 2010) have shown that aerobic exercise training led to increase the DMN (Default Mode Network), which includes the posterior cingulate, ventral and superior frontal medial cortices, and bilateral lateral occipital, middle frontal, hippocampal and parahippocampal, and middle temporal cortices (Fox et al. 2005). Previous studies have also revealed that the enhanced DMN was associated with better memory performance (Hampson et al. 2006) and better performance of executive functions (Andrews-Hanna et al. 2007).

Based on the neuroimaging evidence, the improvements of executive functions, processing speed, and episodic memory can be explained as follows. First, the combination exercise training would increase the BDNF, IGF-1, and VEGF levels. Second, the increased BDNF, IGF-1, and VEGF levels might contribute to exercise-induced neurogenesis and angiogenesis. Third, the neurogenesis and angiogenesis would engender changes in the brain structure, brain function, and brain connectivity, which are related to some cognitive functions. Finally, the improvements of executive functions, processing speed, and episodic memory can be expected to be enhanced by increasing the brain volume in the hippocampus, which is related to memory, greater activity in the middle frontal gyrus which is important for executive functions and processing speed, and enhancing the DMN, which is associated with executive functions and memory through the combination exercise training. No direct evidence supports the hypothesis described above. Future research is needed to investigate brain plasticity after combination exercise training.

The combination exercise training showed no improvement of scores in QOL-26. The possibility exists that scores of the QOL-26 are close to the maximum or the highest scores because we recruited very healthy

elderly people (see “[Inclusion and exclusion criteria](#)”), which means that the participants felt high QOL before the intervention period. Consequently, the present short-term intervention did not improve the QOL of the intervention group compared to that of the control group. Moreover, the 4-week intervention period might not be sufficient to improve mental health. One important future direction for research in this area is to examine whether or not the combination exercise training can improve mental health. To investigate this issue, further study will be necessary with recruitment of nonhealthy older adults or with a long-term intervention period.

This study has several strengths in its methods and results compared to earlier studies using exercise training for elderly people. First, this study used diverse cognitive function measures simultaneously. Therefore, it was possible to show the beneficial effects of the short-term combination exercise training on diverse cognitive functions such as executive functions, episodic memory, and processing speed. Second, training periods (30 min per day, 3 days for 4 weeks) in our combination exercise training were shorter than those of previous exercise training studies. Considering reduced costs for elderly people, shorter intervention studies using exercise training are also needed. Consequently, our short-term combination exercise training offers important suggestions for methods used in the exercise training, in cognitive rehabilitation and in the prevention of dementia.

An important limitation of this study is that we did not use an active control group participating in exercise programs of other types. The reasons for using the waiting list control group are presented in the “[Method](#)” section. From a study design point of view, using the waiting list control group is better than using an active control group. This report is the first describing a study demonstrating the beneficial effects of the combination exercise training on cognitive functions. In the future, we expect to conduct a new intervention study that compares combination exercise training to other exercise training or other cognitive training.

In summary, this report is the first describing a study assessing the beneficial effects of short-term combination exercise on diverse cognitive functions in elderly people. Results showed the beneficial effect of the combination exercise training on executive function, episodic memory, and processing speed. Given that most cognitive functions decrease with age (Yakhno et al. 2007; Royall et al. 2004; Salhouse 1996) and that

these functions are correlated strongly with daily life activities (Cahn-Weiner et al. 2000; Owsley and McGwin 2004), our results elucidate the positive effects of exercise training for elderly people.

Acknowledgments This study was an industry–academic collaboration of Tohoku University, namely Smart Aging Square (<http://www2.idac.tohoku.ac.jp/dep/saarc/square.html>). We thank H. Saito, T. Nakajima, and H. Tsuda for recruiting participants, testers for performing psychological tests, Curves staff members for conducting the combination exercise training, the participants, and our other colleagues in IDAC, Tohoku University for their support.

Ethics statement Ethical approval was provided by the Institutional Review Board of the Tohoku University Graduate School of Medicine (ref. 2011-58). Based on the Declaration of Helsinki, written informed consent was received from each participant.

Conflict of interest All authors have declared no competing interests. This study was supported by Curves Japan Co., Ltd. Funding sources of the trial had no involvement in the study design, collection, analysis, interpretation of data, or writing of the papers.

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