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The Mental Activity and eXercise (MAX) Trial: A Randomized, Controlled Trial to Enhance Cognitive Function in Older Adults

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Abstract

Background—The prevalence of cognitive impairment and dementia are projected to rise dramatically over the next 40 years, and strategies for maintaining cognitive function with age are critically needed. Physical or mental activity alone result in relatively small, domain-specific improvements in cognitive function in older adults; combined interventions may have more global effects.

Methods—We performed a randomized, controlled trial to examine the combined effects of physical plus mental activity on cognitive function in 126 community-residing older adults with cognitive complaints. All subjects engaged in home-based mental activity (1 hour/day, 3 days/week) plus class-based physical activity (1 hour/day, 3 days/week) for 12 weeks and were randomized to either mental activity intervention (MA-I, intensive computer) or mental activity control (MA-C, educational DVDs) plus exercise intervention (EX-I, aerobic) or exercise control (EX-C, stretching/toning) using a 2×2 factorial design so that there were 4 groups: MA-I/EX-I, MA-I/EX-C, MA-C/EX-I, MA-C/EX-C. The primary outcome was global cognitive change based on a comprehensive neuropsychological test battery. Analyses were intent-to-treat using repeated measures random effects regression.

Results—Subjects had a mean age of 73 years; 65% were women and 35% Hispanic or non-white. There were no significant differences between the groups at baseline. Global cognitive scores improved significantly over time (mean 0.16 standard deviations [SD]; p<0.001) but did not differ between groups when comparing MA-I to MA-C (ignoring exercise, p=0.17), EX-I to EX-C (ignoring mental activity, p=0.74), or across all four randomization groups (p=0.26).

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Conclusions—In inactive older adults with cognitive complaints, 12 weeks of physical plus mental activity was associated with significant improvements in global cognitive function with no evidence of difference between intervention and active control groups. These findings may reflect practice effects or may suggest that the amount of activity is more important than the type in this subject population.

Background

Over the next 40 years, it is anticipated that there will be an epidemic of dementia worldwide, with a three- to four-fold increase in the number of prevalent cases due to longer life expectancies and demographic changes.[1] Current treatments provide some symptomatic relief but do not alter the course of the disease,[2] and several therapies that initially appeared promising have recently failed in Phase III clinical trials.[3-5] Attention is turning toward identification of preclinical disease and development of treatments to prevent or delay dementia onset;[6] however, there is also concern about potential side effects of pharmacological treatment in individuals who may never become symptomatic. Behavioral interventions offer a potential strategy to prevent or delay dementia onset with minimal side effects in asymptomatic individuals.

There is growing evidence that both physical and mental activity can improve cognitive function in the short term and may lower the risk of developing dementia over the long term. Numerous observational studies[7-17] and several systematic reviews[18-20] have found that older adults who engage in mental or physical activity are less likely to experience cognitive decline or develop dementia, and several have suggested that physical and mental activity may have independent or additive effects.[7, 11] However, randomized, controlled trials (RCTs) are needed to establish a clear causal relationship between engaging in physical or mental activity and cognitive benefits.

To date, RCTs of physical and mental activity interventions have had mixed results.[21] Mental activity interventions in both healthy elders[22, 23] and individuals with mild cognitive impairment (MCI)[24, 25] have typically found domain-specific improvements, in which benefits are observed in the specific cognitive activities trained with little evidence of generalization to other activities or domains. Exercise interventions in both healthy elders[26, 27] and individuals with MCI[28-30] have found that both aerobic exercise and resistance training are associated with small to moderate improvements in cognitive function, particularly measures of attention, processing speed and executive function.[31-33]

Taken together, these studies suggest that behavioral interventions that combine physical and mental activity may have more global effects than either physical or mental activity alone. However, few RCTs have studied the effects of physical and mental activity together.[34] Therefore, we performed an RCT with a 2×2 factorial design to compare the effects of different physical and mental activity combinations on cognitive function in community-residing older adults with self-reported cognitive complaints.

Methods

Participants

Study participants were recruited primarily through direct mailing to the neighborhoods adjacent to the intervention site (Stonestown YMCA, San Francisco, CA), as well as advertisements, fliers, physician and friend referrals, and recruitment databases. Inclusion criteria were age ≥ 65 years, cognitive complaint (defined as answering ‘yes’ to the question “Do you feel that your memory or thinking skills have gotten worse recently?”), English language fluency, not currently engaging in aerobic exercise or intensive computer training (≤2 days/week, ≤30 minutes/session in the past 3 months) and not planning to travel > 1 week during the study period. Exclusion criteria were dementia (based on self-report, physician diagnosis or scoring ≤ 18 on the modified Telephone Interview for Cognitive Status[35]), other neurological or major psychiatric disorder, significant heart or lung disease, limited life expectancy, or other factors that could potentially limit ability to participate fully in the intervention.

All study procedures were approved by the Committee on Human Research at the University of California, San Francisco, and the Research and Development Committee at the San Francisco Veterans Affairs Medical Center. All subjects provided written informed consent and received physician approval to participate.

Interventions

Study participants were randomized to both a home-based mental activity intervention (MA-I) or mental activity control (MA-C) group plus a class-based exercise intervention (EX-I) or exercise control (EX-C) group using a 2×2 factorial design (Figure 1). Active control groups were utilized to account for the effects of factors such as interaction with a computer and social interaction during a group exercise class.

Mental Activity—All participants were provided with detailed written and in-person verbal instructions regarding their assigned mental activities, which were performed independently at home on a computer for 60 minutes/day, 3 days/week for 12 weeks. The MA-I group performed games designed to enhance the speed and accuracy of visual and auditory processing (Posit Science Corporation, San Francisco, CA). For the first 6 weeks, games focused on visual tasks including determining the direction of visual ‘sweeps’, identifying bird pairs, tracking the location of moving ‘gems’ and identifying targets in peripheral vision. For the second 6 weeks, games focused on auditory tasks including determining the direction of auditory ‘sweeps’, distinguishing between similar sounds, matching sound pairs, recalling a series of sounds, following verbal instructions and answering questions about verbal stories. Program difficulty adjusted automatically and continuously based on each participant's level of performance to maintain a ‘correct’ response level of approximately 85%.

The MA-C group watched educational lectures on art, history and science on DVDs. After each session, participants answered approximately six paper-based, multiple choice or short answer lecture-specific questions. Participants watched the DVDs on a computer for 60 minutes/day, 3 days/week for 12 weeks to match the conditions of the MA-I group.

Exercise—All participants attended study-specific group exercise classes at a local YMCA for 60 minutes/day, 3 days/week for 12 weeks. The EX-I class consisted of 10 minutes warm-up, 30 minutes aerobic exercise (traditional dance-based aerobics format), 5 minutes cool-down, 10 minutes strength training, and 5 minutes stretching/relaxation. Heart rate was monitored by having participants check their wrist or neck pulse for 10 seconds at the beginning, peak and end of class and record the values in an exercise journal, with a target peak heart rate of 60-75% of maximum for age.

The EX-C class consisted of 10 minutes warm-up, 30 minutes stretching and toning, 10 minutes strength training, and 10 minutes relaxation. Heart rate was monitored in the same manner, with a goal of not raising heart rate above resting levels. All classes were taught by a single, certified exercise instructor with experience conducting classes in the elderly with a maximum of 12 subjects per class at any given time.

Compliance and adverse events were monitored using weekly journals and bi-weekly telephone check-ins, and motivational counseling was provided if compliance fell below 80%. Daily attendance was also recorded for the exercise classes.

Randomization and Blinding

Subjects were randomized in blocks of four. The randomization sequence was prepared in advance using a random number generator on a computer. Research staff involved with enrollment and outcome assessment were unaware of the randomization sequence and blinded to group assignment. Study participants were unaware of study hypotheses and were told that the goal of the study was to compare the effects of different physical and mental activity programs.

Outcomes

Primary outcome—The primary outcome of the study was 12-week change in cognitive function based on a composite score from a comprehensive neuropsychological test battery. Specific tests were selected because they have good validity and reliability and are sensitive to cognitive decline in older adults and included measures of verbal learning and memory (Rey Auditory Verbal Learning Test [RAVLT]),[36] verbal fluency (letter and category),[37] processing speed (Digit Symbol Substitution Test [DSST]),[38] executive function/mental flexibility (Trail-Making Test, Parts A & B),[39] executive function/inhibition (Eriksen Flanker Test [EFT] congruent and incongruent reaction times),[40] and visuospatial function (Useful Field of View [UFOV] processing speed, divided attention and selective attention).[41]

The Modified Mini-Mental State Examination (3MS)[42] was performed at baseline only to assess global cognitive status (range: 0-100).

A composite cognitive score was created by converting all individual cognitive scores to standardized z-scores by subtracting the baseline group mean and dividing by the baseline group standard deviation (SD) and averaging them. For tests with more than one component (e.g., Trails A & B), the component scores were averaged prior to calculating the composite score so that all tests were weighted equally. In subjects who were missing data for three or fewer cognitive tests, the composite score was based on non-missing tests.

Other measures—Demographic measures included age, sex, race/ethnicity and income. Comborbid medical conditions were determined based on self-report of prior physician diagnosis. Physical performance was assessed with the Senior Fitness Test,[43] which includes standard measures of chair stand, arm curl, 2-minute step test, sit-and-reach, back scratch, and 8-foot up-&-go.

Power

Our study had 80% power to detect an effect size of approximately 0.3 SDs when examining the main effects of MA-I vs. MA-C (ignoring exercise) and EX-I vs. EX-C (ignoring mental activity) (n=63/group) and an effect size of 0.45 SDs when comparing across the 4 randomization groups (n=31/group), assuming 80% correlation between measures within subjects and using two-sided alpha=0.05.

Analyses

All analyses were intent-to-treat. Baseline characteristics were compared between groups using Chi-square for categorical variables and analysis of variance (ANOVA) for continuous variables. Mixed effects linear regression models were utilized to examine change in cognitive scores as a function of randomization group, time (baseline or post-intervention), and the group by time interaction.[44] Random intercepts for each subject were utilized to model correlation between subjects over time. Robust estimation of the variance/covariance structure was used to account for the possibility of unequal variance at the two time points. Due to the factorial design, analyses were performed to compare MA-I vs. MA-C (ignoring exercise) and EX-I vs. EX-C (ignoring mental activity) as well as all four randomization groups. Analyses were performed using the xtreg command in Stata 12 (StataCorp LP, College Station, TX).

Secondary analyses examined the impact of the interventions on individual cognitive tests. Based on prior studies,[45, 46] we hypothesized a priori that the effects of EX-I would be greatest for measures of executive function, especially the Eriksen Flanker incongruent task, and that the effects of the MA-I would be greatest for the Useful Field of View test, which is similar to one of the games in the training program.

To help interpret the main results of the study, we also performed two post-hoc sub-group analyses to assess whether associations differed as a function of low memory (defined as delayed recall ≤5 words [≥1 SD below the mean] on the RAVLT) or poor physical function (defined as <65 full steps on the two-minute step test) at baseline by including 3-way interaction terms for these variables, randomization group and time in the random effects regression models.

All results were similar when analyses were restricted to subjects who completed the study; therefore, only intent-to-treat results are shown.

Results

The flow of participants through the study is shown in Figure 2. Subjects were enrolled from January 2008 to September 2009, and data collection was completed in December 2009. A total of 688 individuals contacted us for more information and were assessed for eligibility. Of these, 562 were excluded (359 did not meet eligibility criteria, primarily due to high levels of current physical activity; 151 declined to participate, primarily due to lack of interest or time; 51 contacted us after the study had been closed; and 1 withdrew prior to baseline) and 126 were enrolled. Thirty-two participants were randomized to the MA-I/EX-I group (intensive computer/aerobic exercise), 31 to the MA-I/EX-C group (intensive computer/stretching&toning), 31 to the MA-C/EX-I group (DVDs/aerobic) and 32 to the MA-C/EX-C group (DVDs/stretching).

A total of 26 (21%) subjects withdrew during the study: 8 developed an illness, 5 were physically unable to perform the study activities, 3 were not approved by their physician, 4 cited time constraints, 5 cited personal reasons such as a family member's illness, and 1 was dissatisfied. Withdrawals did not differ significantly between the MA-I and MA-C groups, the EX-I and EX-C groups, or all four randomization groups.

In addition, 9 (7%) of subjects experienced an adverse event that was considered possibly or probably study related (4 pain, 2 falls, 2 dizziness, 1 hospitalization for pulmonary edema). All subjects recovered without residual problems.

Baseline characteristics of study participants by randomization group are shown in Table 1. Overall, participants had a mean age of 73 years and 16 years of education; 63% were women and 35% were Hispanic or non-white. Participants had relatively high global cognitive function (mean 3MS, 94.4). Fifty-six percent had hypertension, 13% had diabetes mellitus, 9% had previously had a myocardial infarction; and 52% were current or former smokers. There were no significant differences in baseline characteristics between the MA-I or MA-C groups, the EX-I or EX-C groups, or all four randomization groups.

Baseline cognitive test scores by randomization group are shown in Table 2. On average, study participants had moderate to high levels of cognitive function at baseline, consistent with their age and education levels. There were no significant differences in baseline cognitive test scores between the MA-I or MA-C groups, the EX-I or EX-C groups, or all four randomization groups.

The impact of the interventions on our primary outcome of cognitive change in the composite score is shown in Figure 3. There was a significant main effect of time indicating significant improvement over all of the groups (mean, 0.16 SDs; $p<0.001$). However, there were no significant differences when we compared MA-I vs. MA-C ($p=0.17$), EX-I vs. EX-C ($p=0.74$), or all four randomization groups ($p=0.26$).

When we examined individual cognitive tests, there were significant main effects for time for the DSST, Trails A, EFT congruent and incongruent, and UFOV divided and selective attention, with trends toward improvement on most other tests except delayed recall on the RAVLT (Figure 4). The only significant differences between the groups were observed for the UFOV divided and selective attention tasks, which improved more in the MA-I than the MA-C group (Table 3).

Approximately 27% (n=34) of subjects had low memory scores at baseline. The 3-way interaction between baseline memory, mental activity group and time was of borderline statistical significance (p=0.054) and, in subjects with low memory, the difference in cognitive change between the MA-I and MA-C groups was also of borderline statistical significance (p=0.08) (Figure 5). There was no evidence of interaction between baseline physical function, randomization group and time (data not shown).

Comment

In this 2×2 factorial RCT examining the effects of different physical and mental activity interventions on cognitive function in non-demented, inactive elders with cognitive complaints, we found that cognitive scores improved significantly over 12 weeks, but there were no significant differences between the intervention and active control groups. These results may suggest that, in this study population, the amount of activity is more important than the type of activity, since all groups participated in both mental activity and exercise for 60 minutes/day, 3 days/week for 12 weeks. Alternatively, the cognitive improvements observed may be due to practice effects.

To assess the possibility that our results were due to practice, we recruited an additional 12 subjects to participate in a no-contact control study in which all study procedures were identical except that there was no intervention. Composite cognitive test scores in these subjects improved 0.08 SDs, compared with 0.16 SDs in the main study, suggesting that some, but not all, of the improvements observed may have been due to repeated testing.

Our findings differ from prior RCTs, which have found that a similar intensive computer training program improved cognitive function more than educational DVDs in healthy elders.[46, 47] It is possible that this is attributable to differences in the outcome measures used or the manner in which the intervention was implemented. Consistent with prior studies, we found that the MA-I training yielded significantly greater improvements in those cognitive tests that were similar to the training program.[22, 23]

We did not observe any differences between the EX-I (aerobic) and EX-C (stretching/toning) groups for either global cognitive function or individual cognitive tests. This differs from prior RCTs in healthy elders, which have found that aerobic exercise improves cognitive function and increases hippocampal volume when compared with stretching/toning.[26, 48, 49] It is possible that our 12-week intervention was not long enough or intense enough to achieve a substantially greater aerobic response in the intervention group, and that a difference between the groups would have emerged in a longer study. It also is possible that subjects in the stretching/toning group engaged in more aerobic activities outside of the study as a function of their participation and readiness to exercise. Alternatively, it is possible that, in our study population of older adults with cognitive complaints, both aerobic exercise and stretching/toning resulted in physical changes that were equally beneficial. This hypothesis is supported by other recent RCTs that have found resistance training alone is associated with improvements in executive function.[27, 29]

Strengths and limitations

Our study had several key strengths, including the 2×2 factorial design and the use of active control conditions, which enabled us to control for factors such as social interaction during the group exercise class and mental stimulation associated with using a computer. However, there is growing evidence that even these less intensive interventions may have cognitive and physical benefits in older adults.[50,51] Future studies should consider inclusion of both active and no-contact control conditions.

Our study also has several potential limitations. Although more than one-third of participants were Hispanic or non-white, most were highly educated, raising concern about the generalizabililty of the findings. In addition, our study did not include objective measures of aerobic fitness such as peak oxygen consumption; therefore, we cannot be sure that subjects in the EX-I group achieved improvements in aerobic fitness. Our cognitive test battery also did not include the Digit Span test, which was found in a recent review to be most consistently affected by exercise.[33] Finally, we did not perform a full clinical evaluation on study participants.

Conclusion

In inactive elders with cognitive complaints, 12 weeks of a combined mental activity and exercise program was associated with significant improvements in global cognitive function with no evidence of difference between intervention and active control groups. These findings may reflect practice effects or may suggest that the amount of activity is more important than the type in this subject population.

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Dr. Barnes had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analyses.

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http://clinicaltrials.gov/ct2/show/NCT00522899.

Full trial protocol available upon request from Dr. Barnes.

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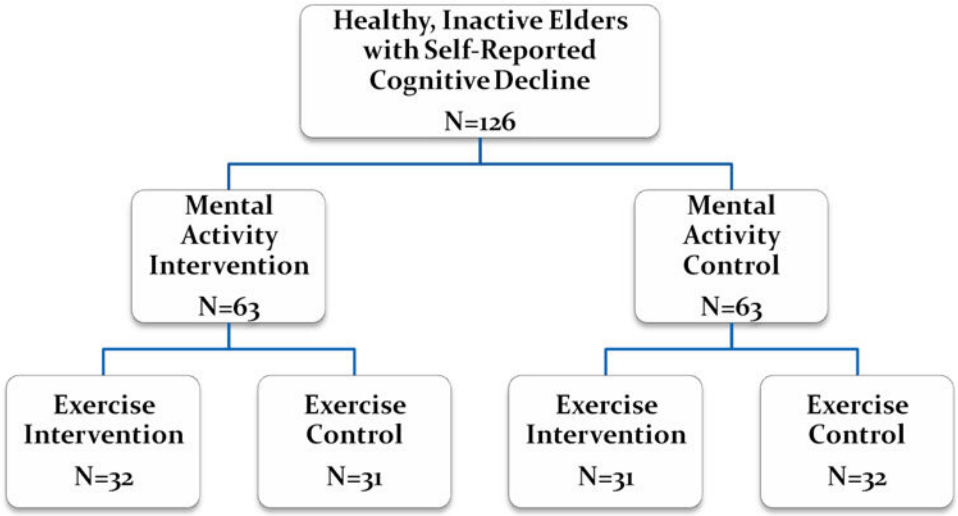

Figure 1.

Mental Activity and eXercise (MAX) Trial Design.

The MAX Trial used a 2×2 factorial design in which subjects were first randomized to either the mental activity intervention (MA-I: intensive computer training) or mental activity control (MA-C: educational DVD) group and then to the exercise intervention (EX-I: aerobic) or exercise control (EX-C: stretching/toning) group. This design enables comparisons to be made between the mental activity groups (ignoring exercise) and between the exercise groups (ignoring mental activity) and also to assess for evidence of interaction between mental activity and exercise.

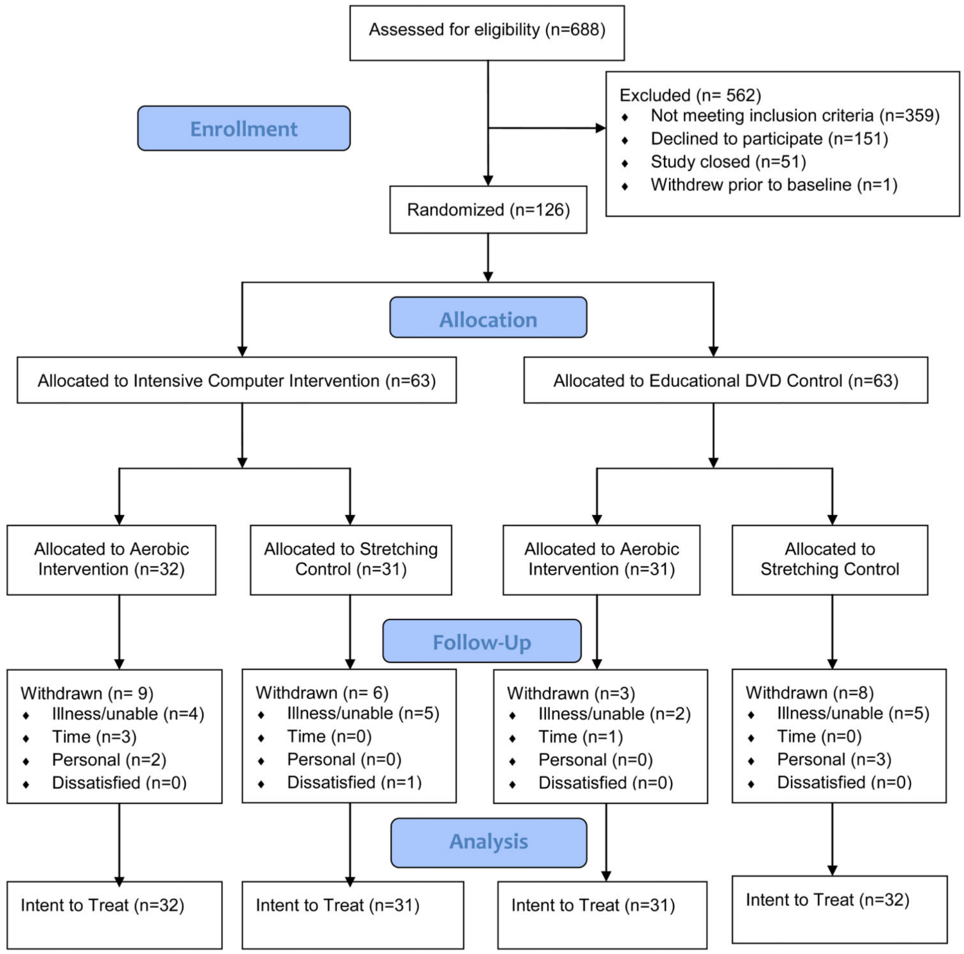

Figure 2.
Flow Chart

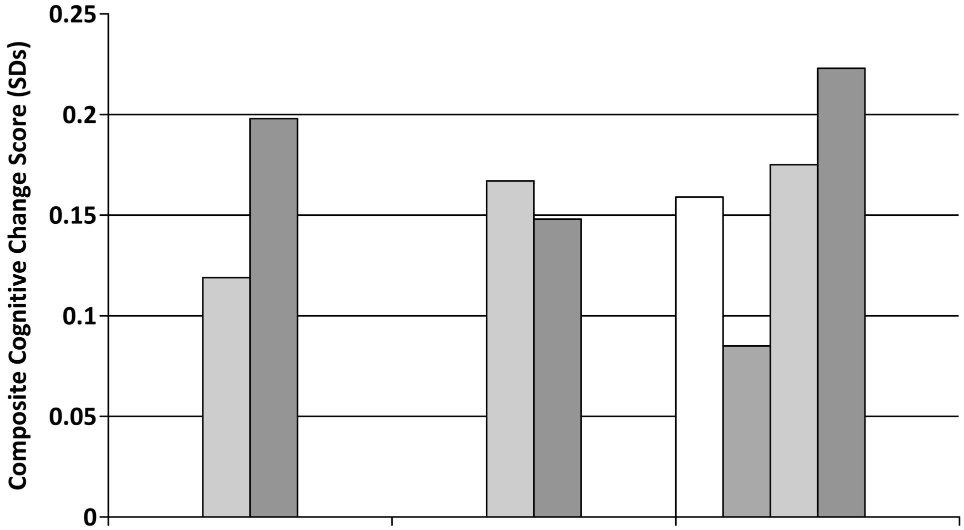

Figure 3. Impact of Intervention on Composite Cognitive Score

For the primary outcome of change on the composite cognitive score, scores improved significantly over time but did not differ between the MA-I and MA-C groups, EX-I and EX-C groups or all 4 randomization groups.

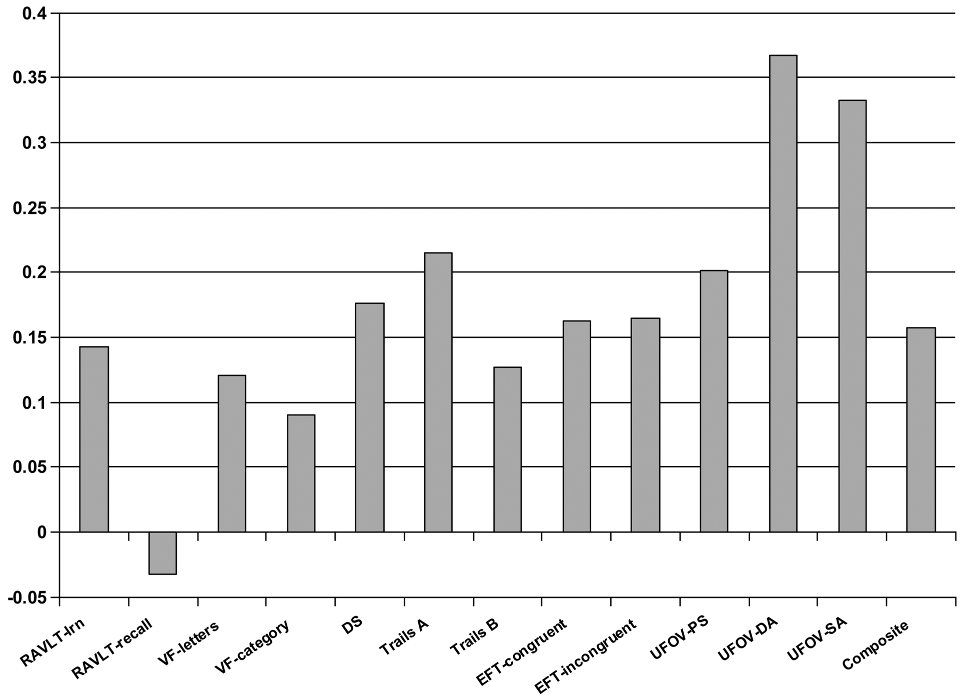

Figure 4. Change in Individual Cognitive Tests

Cognitive function improved significantly ($p<0.05$) for the Digit Symbol Substitution Test (DSST), Trails A, Eriksen Flanker Test (EFT) congruent and incongruent tests, and Useful Field of View divided attention (UFOV-DA) and selective attention (UFOV-SA), and composite score. Improvements were of borderline statistical signficance ($p<.10$) for Rey Auditory Verbal Learning Test total words learned (RAVLT-lrn), Trails B, and UFOV processing speed (UFOV-PS).

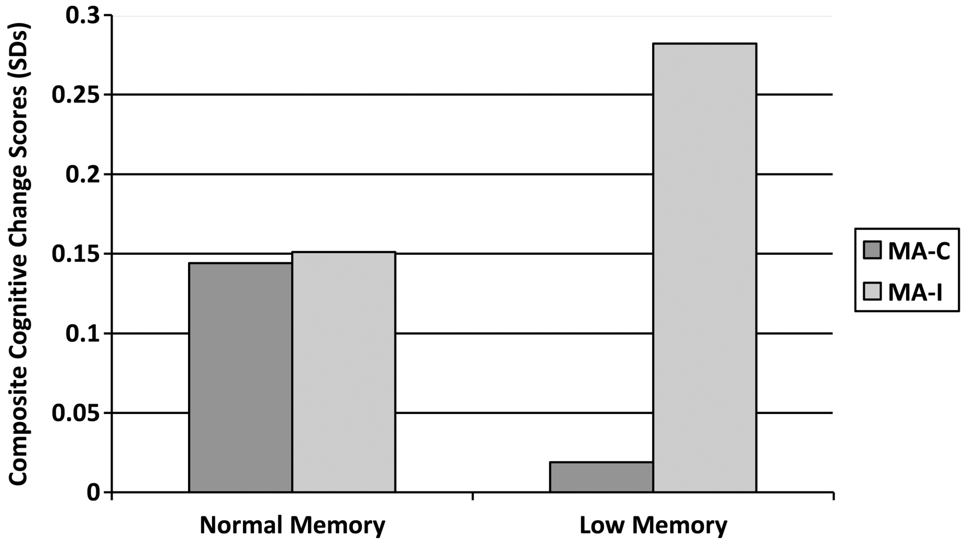

Figure 5. Comparison of Mental Activity Intervention (MA-I) versus Mental Activity Control (MA-C) Groups in Subjects With Normal Memory and Low Memory

Figure 5 show the three-way interaction between baseline memory, mental activity group and time and raises the possibility that the mental activity intervention (MA-I) training may have led to greater cognitive improvements than the mental activity control (MA-C) training in subjects with low memory at baseline, although the interaction and the between-group effects were both of borderline statistical significance.

Table 1

Baseline Characteristics of 126 Study Participants by Randomization Group*

	Mental Activity Control		Mental Activity Intervention		
Characteristic	**Exercise Control (n=32)**	**Exercise Intervention (n=31)**	**Exercise Control (n=31)**	**Exercise Intervention (n=32)**	**p-value**
Age, years	73.9 (6.3)	71.1 (5.5)	73.8 (5.7)	74.8 (6.1)	0.08
Gender, female	20 (62.5)	21 (67.7)	18 (58.1)	20 (62.5)	0.89
Education, years	16.3 (2.1)	15.6 (2.8)	16.8 (2.3)	16.7 (2.2)	0.18
Race/ethnicity, non-Hispanic white	22 (68.8)	17 (54.8)	22 (71.0)	21 (65.6)	0.55
Global cognition (3MS)	94.8 (4.7)	94.6 (5.6)	94.4 (3.9)	94.0 (5.2)	0.92
Hypertension	17 (53.1)	20 (64.5)	14 (45.2)	19 (59.4)	0.45
Diabetes	5 (15.6)	5 (16.1)	4 (12.9)	3 (9.4)	0.85
Myocardial infarction	4 (12.5)	2 (6.5)	3 (9.7)	2 (6.3)	0.79
Current/former smoker	16 (53.3)	18 (58.1)	12 (40.0)	16 (51.6)	0.54

*Values reflect mean (standard deviation) or number (percent). P-values based on analysis of variance or Chi-square test across the four groups. Data missing as follows: education (n=3), race/ethnicity (n=1), smoking status (n=4). 3MS, Modified Mini-Mental State Examination. No significant differences between the mental activity intervention and mental activity control groups (ignoring exercise), exercise intervention and exercise control groups (ignoring mental activity), or all four randomization groups.

Table 2

Baseline Cognitive Scores by Randomization Group

Cognitive Test*	Mental Activity Control		Mental Activity Intervention		p-value
	Exercise Control (n=32)	Exercise Intervention (n=31)	Exercise Control (n=31)	Exercise Intervention (n=32)	
Verbal learning & memory (RAVLT)					
No. words learned	41.0 (8.9)	41.5 (9.0)	40.0 (9.9)	41.2 (10.2)	0.93
No. words recalled	7.3 (2.6)	8.3 (2.8)	7.2 (4.1)	7.1 (2.9)	0.47
Verbal fluency					
No. words, letter	12.8 (3.7)	12.4 (5.3)	12.6 (4.0)	12.8 (4.6)	0.98
No. words, category	18.9 (5.1)	18.3 (5.1)	17.2 (5.4)	18.6 (4.4)	0.55
Processing speed (DSST)					
No. correct	55.7 (13.9)	58.1 (13.9)	54.8 (14.6)	56.6 (11.0)	0.80
Executive function/mental flexibility					
Trails A, seconds	41.6 (15.3)	37.2 (14.5)	36.5 (17.1)	44.4 (14.8)	0.16
Trails B, seconds	100.9 (47.6)	102.9 (56.9)	94.7 (46.4)	87.6 (31.1)	0.58
Executive function/inhibition (EFT)					
Congruent reaction time, milliseconds	622.2 (113.0)	600.8 (153.7)	612.8 (116.1)	659.2 (136.5)	0.34
Incongruent reaction time, milliseconds	691.1 (135.8)	685.2 (115.7)	700.4 (151.0)	732.6 (147.7)	0.55
Visuospatial function (UFOV)					
Processing speed, milliseconds	33.7 (39.7)	36.5 (49.3)	34.9 (33.3)	34.6 (35.6)	0.99
Divided attention, milliseconds	115.5 (116.1)	129.3 (137.1)	118.4 (116.0)	117.0 (124.3)	0.97
Selective attention, milliseconds	238.9 (107.8)	217.3 (99.6)	228.8 (116.8)	234.3 (107.5)	0.89

* RAVLT, Rey Auditory Verbal Learning Test; DSST, Digit Symbol Substitution Test; EFT, Eriksen Flanker Test; UFOV, Useful Field of View. No significant differences between the mental activity intervention and mental activity control groups (ignoring exercise), exercise intervention and exercise control groups (ignoring mental activity), or all four randomization groups.

Table 3

Standardized Mean Change in Cognitive Scores by Randomization Group

	Mental Activity Control		Mental Activity Intervention		
Cognitive Test*	**Exercise Control (n=32)**	**Exercise Intervention (n=31)**	**Exercise Control (n=31)**	**Exercise Intervention (n=32)**	**p-value**
Composite score	.16 (.05, .26)	.08 (-.004, .17)	.17 (.03, .31)	.22 (.12, .33)	.26
Verbal learning & memory (RAVLT)					
No. words learned	.33 (.09, .58)	.14 (-.14, .43)	.13 (-.11, .37)	-.04 (-.42, .33)	.38
No. words recalled	.01 (-.32, .33)	.02 (-.28, .32)	-.10 (-.36, .16)	-.07 (-.46, .32)	.93
Verbal fluency					
No. words, letter	-.05 (-.33, .24)	.08 (-.21, .37)	.24 (-.11, .58)	.22 (-.15, .58)	.57
No. words, category	.06 (-.26, .38)	-.07 (-.41, .26)	.22 (-.06, .50)	.18 (-.24, .60)	.59
Processing speed (DSST)					
No. correct	.15 (-.02, .32)	.19 (.04, .33)	.27 (.03, .51)	.08 (-.13, .30)	.71
Executive function/mental flexibility**					
Trails A, seconds	-.36 (-.58, -.15)	-.12 (-.32, .07)	-.03 (-.50, .44)	-.36 (-.63, -.08)	.24
Trails B, seconds	-.22 (.45, .002)	-.18 (-.49, .13)	.13 (-.21, .48)	-.25 (-.51, .01)	.31
Executive function/inhibition (EFT)**					
Congruent reaction time, milliseconds	-.17 (-.51, .16)	.01 (-.42, .43)	-.17 (-.41, .06)	-.33 (-.55, -.11)	.51
Incongruent reaction time, milliseconds	-.12 (-.36, .12)	-.07 (-.48, .33)	-.15 (-.52, .22)	-.33 (-.58, -.08)	.60
Visuospatial function (UFOV)**					
Processing speed, milliseconds	-.23 (-.66, .19)	-.04 (-.43, .34)	-.17 (-.61, .26)	-.39 (-.77, -.02)	.65
Divided attention, milliseconds	-.13 (-.48, .22)	-.17 (-.39, .05)	-.60 (-.99, -.22)	-.62 (-.97, -.26)	.05
Selective attention, milliseconds	-.18 (-.59, .22)	-.14 (-.43, .16)	-.34 (-.58, -.11)	-.71 (-.96, -.46)	.02

* RAVLT, Rey Auditory Verbal Learning Test; DSST, Digit Symbol Substitution Test; EFT, Eriksen Flanker Test; UFOV, Useful Field of View. Significant differences between mental activity intervention and mental activity control groups for UFOV-divided attention and UFOV-selective attention. No other significant differences between mental activity intervention and mental activity control groups (ignoring exercise), exercise intervention and exercise control groups (ignoring mental activity), or all four randomization groups.

** For timed tests, negative change reflects improvement (i.e., faster performance).