Cognitive Effects of Adding Caloric Restriction to Aerobic Exercise Training in Older Adults with Obesity

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Objective: This study examined the short- and long-term effects of adding caloric restriction to 5 months of aerobic exercise training on executive function in sedentary older adults with obesity.

Methods: Sedentary adults with obesity aged 65 to 79 years completed a randomized trial investigating the cardiorespiratory benefits of adding moderate (~250 kcal) or high (~600 kcal) caloric restriction to a 20-week aerobic exercise program. Approximately half (n=88) completed a cognitive assessment battery at baseline, post intervention, and 18 to 24 months after intervention completion. The primary outcome was an executive function composite score.

Results: In the overall sample, the executive function composite increased 0.114 from baseline to postintervention (P=0.01). Randomization to caloric restriction did not significantly alter executive function over aerobic exercise alone, nor were there between-group differences on any individual executive function test following the intervention or at long-term follow-up. Adding caloric restriction to exercise was associated with a modest increase in Mini-Mental State Examination score (P=0.04). In the overall sample, increases from baseline at long-term follow-up were noted in digit symbol and word list recall performance as well.

Conclusions: Adding caloric restriction to a 20-week aerobic exercise program does not worsen or improve executive function more than exercise alone assessed up to 24 months post randomization.

Introduction

Strong evidence is emerging that midlife obesity (BMI ≥ 30 kg/m2) is a risk factor for dementia later in life. However, the interplay of obesity and weight loss on cognition after the age of 65 is not as well understood. Epidemiological studies have indicated that weight loss in older age is associated with poorer cognition (for reviews, see (1-3)). However, it is difficult to disentangle whether unintentional weight loss in older age is a risk factor for, or marker of, dementia (2).

Recommendations to achieve weight loss emphasize increasing physical activity and reducing caloric intake (4). Evidence is strong that regular aerobic exercise benefits cognition in older adults, particularly executive function (EF) (5-8). Since work showing that aerobic exercise enhances synaptic plasticity in an adult rodent model (9), human primate (20) studies have shown direct benefits of CR on the brain, including preservation of synaptic plasticity and brain volumes.

Adding caloric restriction (CR) to aerobic exercise can potentiate the benefits of exercise on cardiorespiratory fitness in older adults with obesity (14-16). CR literature in aging suggests intentional weight loss should promote neurocognitive health by improving insulin sensitivity and reducing fat mass, blood lipids, and inflammatory markers, all of which have been negatively associated with brain health in human studies (for a review, see ((18))). In addition, rodent (19) and nonhuman primate (20) studies have shown direct benefits of CR on the brain, including preservation of synaptic plasticity and brain volumes.

In spite of this compelling evidence, few well-controlled studies of exercise and CR in older adults with obesity have been published. One well-controlled study indicated that combined exercise and CR over 6 to 12 months may benefit cognition more than CR alone but not more than...
exercise alone (21). In contrast, results from the less well-controlled but better-powered Action for Health in Diabetes (Look AHEAD) trial suggest that intensive lifestyle interventions combining weight loss and exercise in older adults with obesity and type 2 diabetes may be detrimental to cognition long term (22).

We tested the effects on EF of adding CR to aerobic exercise by including EF tests in a trial investigating whether adding CR to a 20-week aerobic exercise intervention (14) could potentiate benefits of aerobic exercise on cardiorespiratory fitness (peak oxygen consumption [VO2] \(\text{VO}_2\)) in sedentary older adults with obesity. We hypothesized that adding CR to aerobic exercise would enhance the benefits of aerobic exercise on EF in older adults with obesity.

**Methods**

**Overall study design**

This study was ancillary to the Investigating Fitness Interventions in the Elderly (INFINITE) trial (ClinicalTrials.gov identifier NCT01048736), a 20-week, three-group, single-blind randomized controlled trial in 180 men and women aged 65 to 79 years old from Forsyth County, North Carolina, and surrounding regions (14). Participants were randomized to exercise only (Ex Only), exercise plus moderate CR (Ex + Mod CR), or exercise plus high CR (Ex + High CR). As part of the ancillary study, the last 88 participants randomized into the parent study completed a cognitive assessment battery focused primarily on EF before and after the intervention. Of these 88, 70 participants completed a long-term follow-up visit that occurred 18 to 24 months after intervention completion. During this visit, participants repeated the cognitive assessment battery, blood was drawn to assess serum lipids and glucose, and anthropometric measurements were obtained. The study was approved by the Wake Forest School of Medicine Institutional Review Board and was completed in accordance with the Declaration of Helsinki. All participants provided written, informed consent prior to study participation.

**Participants**

The sample in this analysis is 88 participants who completed the baseline and postintervention EF battery. All participants randomized after November 28, 2011, were included in the ancillary. Participants were 65 to 79 years old (mean [SD] = 69.0 [3.5]), had BMI of 30 to 45 kg/m² (mean = 35.3 [3.9]), were weight stable (<5% weight change in past 6 months), and were sedentary (self-reporting <20 minutes of exercise three times per week, including walking, in the past 6 months). Exclusion criteria included Mini-Mental State Examination (MMSE) score < 24; osteoporosis; smoking within the past year; insulin-dependent diabetes; hip fracture, hip or knee replacement, or spinal surgery in the previous 6 months; clinical evidence of depression, heart disease, cancer, liver disease, renal disease, chronic pulmonary disease, uncontrolled hypertension, or major physical impairment; or contraindication for exercise or weight loss upon examination. All participants were approved for study participation by the study physician (ML). Participant characteristics are provided in Table 1. A comparison of characteristics in this sample with the full study cohort is presented in Supporting Information Table S1.

**Interventions**

**Aerobic training.** All participants completed the same aerobic exercise intervention, designed in accordance with the American Heart Association and American College of Sports Medicine physical activity recommendation for optimizing cardiovascular fitness in older adults (23). Participants walked on treadmills 4 d/wk for 5 months under the supervision of two exercise interventionists at the research facility to minimize individual variability in compliance and progression and to ensure a similar exercise stimulus across study groups.

Participants warmed up by walking for 3 to 5 minutes at a slow pace. The duration of exercise progressed to 30 minutes at 65% to 75% heart rate reserve by the end of the sixth week and thereafter. Each walking session ended with a 3- to 5-minute cooldown followed by large muscle flexibility exercises. A minimum of two heart rate readings were taken during the exercise session using Polar heart rate monitors to monitor compliance with the prescribed intensity. Treadmill speed and grade were adjusted individually by study staff based on these heart rate values.

**CR.** Participants randomized to the Ex Only group \(n = 28\) were asked to maintain their regular dietary intake. Those assigned to either the Ex + Mod CR \((-250\text{-kcal/d deficit; } n = 30\) or the Ex + High CR \((-600\text{-kcal/d deficit; } n = 30\) groups were provided with a controlled diet consisting of lunch and dinner prepared by the Wake Forest School of Medicine Clinical Research Metabolic Kitchen under the direction of a registered dietitian (RD). Participants picked up their food three times per week and were asked to keep a log of everything they consumed. The logs were reviewed, and body weight was measured weekly by the study RD to verify diet compliance. Brief individual counseling sessions with the study RD were held weekly to facilitate motivation and compliance.

The individual calorie level assigned for each participant was derived by subtracting 250 kcal (“Mod CR”) or 600 kcal (“High CR”) from the participant’s estimated daily energy needs for weight maintenance. Individual daily energy need was calculated from the direct measurement of resting metabolic rate (RMR), applying an activity factor based on each participant’s reported daily activities. RMR was measured after an overnight fast by indirect calorimetry (MGC Diagnostics) (24). At the end of the intervention, RMR was measured again, and participants were provided with a 7-day diet for weight maintenance, during which period postintervention follow-up testing occurred, as described previously (14).

**Outcomes**

All assessments took place in the Geriatric Research Center of the Sticht Center for Healthy Aging and Alzheimer’s Prevention at Wake Forest School of Medicine by examiners blinded to treatment assignment. Baseline assessments took place within 3 weeks prior to starting the interventions. Postintervention follow-up assessments took place during the 2 weeks after the intervention. Long-term follow-up assessments occurred 18 to 24 months after intervention completion.

**Cognitive outcomes.** Cognitive outcomes were measured at baseline, postintervention follow-up, and long-term follow-up. Cognitive tests were administered by a trained study coordinator in a quiet testing room. Prior to completing the cognitive assessment battery, participants were asked whether they had followed their normal daily eating and medication regimens and completed a finger stick glucose test to confirm that blood glucose levels were > 60 mg/dL. All participants presented with glucose levels higher than the cutoff.
The cognitive testing battery included the Digit Symbol Coding (DSC) task, the Trail Making Test (TMT) parts A and B, the Stroop task, phonemic fluency, semantic fluency, and the Rey Auditory Verbal Learning Task (RAVLT). The 90-second version of the DSC task was administered; the outcome was the number of correct responses (25-27). The TMT outcome was difference in time in parts A and B in seconds (28). The interference score (interference score = [(time [s] needed for subtask 3) − (time [s] needed for subtasks 1 + 2)] ÷ 2) from the 40-item version of the Stroop task was used (29,30). For phonemic fluency, participants verbally generated in 1 minute as many words as possible beginning with the letter F and then did likewise for the letters A and S (28). The sum of all three trials was used for analysis. For semantic fluency, participants verbally listed as many animals as possible within 1 minute and then did likewise for kitchen items. The sum of both trials was used for analysis. The RAVLT is a word list memory task (28), and the sum of correctly recalled words across the first five trials was used. Global cognition was tested with the MMSE (31).

A composite score of EF was calculated by summing the $z$ scores of the DSC score, TMT B-A time, Stroop interference score, phonemic fluency, and semantic fluency. The sign of the $z$ score was reversed prior to summing when necessary so that larger $z$ scores indicate better performance.

**Cardiometabolic outcomes.** The primary outcome of the parent study was peak VO$_2$ determined on a motorized treadmill during a graded exercise test to exhaustion using a ramp protocol (14). Fasting and 2-hour postprandial glucose and insulin were measured in blood samples drawn before (0 minutes) and after (120 minutes) a 75-g glucose ingestion. An estimate of insulin resistance by the homeostatic model assessment of insulin resistance (HOMA2-IR) was calculated using the fasting plasma insulin and glucose values as described (32).

**Statistical methods.** This analysis included the 88 participants who had EF composite scores at baseline and from at least one of the two follow-up visits. Baseline characteristics of the participants (Table 1) are described as mean (SD) for continuous variables and as count (percentage) for categorical variables. Unadjusted mean scores for cognitive measures at each visit were calculated for each treatment group (Table 2).

The primary analysis for the ancillary study was to compare the EF $z$ score between treatment groups following the intervention and at long-term follow-up after adjusting for baseline measures using ANCOVA with repeated measures. Similarly, ANCOVA with repeated measures was also
TABLE 2

Unadjusted mean scores for cognitive measures at baseline, postintervention, and long-term follow-up

|                      | Baseline | Postintervention | Long-term follow-up |
|----------------------|----------|------------------|---------------------|
|                      | Ex Only  | Ex + Mod CR      | Ex + High CR        |
|                      | (n=20)   | (n=21)           | (n=21)              |
| Ef composite         | 48.4 (39.2) | 48.7 (38.4)     | 48.5 (38.2)         |
| DSC                  | 0.2 (0.8)   | 0.1 (0.6)         | 0.2 (0.6)           |
| Trails B-A           | 40.1 (33.0) | 40.3 (30.9)      | 40.2 (33.0)         |
| Stroop interference  | 20.1 (4.8)    | 20.6 (4.1)        | 20.5 (4.1)          |
| Semantic fluency     | 12.6 (4.9)   | 12.0 (4.3)        | 11.7 (4.3)          |
| Phonemic fluency     | 40.4 (6.0)    | 40.2 (4.5)        | 40.5 (5.5)          |
| MMSE                 | 27.5 (4.5)    | 27.5 (4.5)        | 27.5 (4.5)          |
| RAVLT                | 52.8 (10.3)   | 52.8 (10.3)       | 52.8 (10.3)         |

No significant differences noted at baseline (all \(P > 0.10\)).

In addition, we used ANCOVA with repeated measurements to evaluate the overall intervention effect (combining all groups) with changes in cognitive scores at postintervention follow-up and long-term follow-up as the dependent variable, adjusted for the covariates in Model 2 (Supporting Information Table S2). An analysis using change in cognitive scores rather than adjusting for baseline is included as Supporting Information Table S3. All analyses were done using SAS software version 9.4 (SAS Institute, Cary, North Carolina). Significance was determined using \(P < 0.05\).

Planned secondary comparisons examined the role of insulin resistance and cardiorespiratory fitness by adding change between baseline and postintervention follow-up in either HOMA2-IR (Model 3) or peak VO\(_2\) (Model 4) to Model 2 to test whether differences in mean cognitive performance were associated with changes in cardiorespiratory fitness or insulin resistance, after adjusting for group assignment. Because individual weight loss and decreases in caloric intake varied, sensitivity analyses were performed to test whether changes in weight loss or decreased caloric consumption were associated with cognitive performance, regardless of group assignment.

Results

Adherence and compliance in the parent study were excellent (87% retention, >85% exercise attendance, and >95% diet compliance) (14). No participant dropped out because of an intervention-related adverse event, and baseline characteristics of those who dropped out were not different from those who completed the study. As in the parent study (14), participants in the Ex + Mod CR (~9.45% [4.50%]) and Ex + High CR (~10.45% [3.97%]) both lost more body mass than Ex Only (~1.13% [3.44%]), and differences in body mass lost between CR groups did not reach statistical significance.

Overall effects of intervention on cognitive outcomes

Raw cognitive scores at baseline, postintervention, and long-term follow-up are shown in Table 2. There were no between-group differences in cognitive performance at baseline (all \(P > 0.10\)). No interactions between group and visit were statistically significant (all \(P > 0.05\)) for Models 1 and 2.

In the overall sample, performance improved by 0.114 on the EF composite between baseline and postintervention follow-up (\(P = 0.01\); 95% CI: 0.028-0.200). The 0.074 improvement in EF between baseline and long-term follow-up was not significant (\(P = 0.10\); 95% CI: ~0.14 to 0.162); however, the difference between postintervention and long-term follow-up EF was not statistically different (\(P > 0.10\)).
TABLE 3  Adjusted mean scores show effects of randomization on cognitive outcomes and at long-term follow-up based on mixed-effect models

| Outcome | P value, group | P value, visit |
|---------|---------------|---------------|
| Ex Only | 0.0430        | 0.0492        |
| Ex + Mod CR | 0.2365    | 0.2365        |
| Ex + High CR | 0.0088     | 0.0088        |

Supporting Information Table S2 shows overall differences following the intervention and at long-term follow-up in the overall sample for all cognitive tests.

Effect of randomization to CR on cognitive outcomes

In both the minimally adjusted model (Model 1) and fully adjusted model (Model 2), randomization to Ex + Mod CR or Ex + High CR compared with Ex Only did not result in significant differences in the EF composite score, nor were there any between-group differences on any individual EF test (Table 3, Figure 1). In both Model 1 and Model 2, there was a modest association ($P = 0.04$) between group assignment and MMSE score, with those randomized to Ex + High CR having slightly higher global cognition scores compared with Ex Only.

Effect of visit time point on cognitive outcomes

There was not a significant effect of visit time point (post intervention vs. long term) for the EF composite score. This reflects the result reported above that the EF composite score increased post intervention in all three groups and was not statistically different between postintervention and long-term follow-up. There were statistically significant effects of time point for both the DSC ($P = 0.0008$) and RAVLT ($P = 0.0010$) using Model 1 that were maintained or strengthened using Model 2 (DSC: $P = 0.0008$; RAVLT: $P = 0.0095$). This reflects that, in the overall sample, the DSC task showed a nonsignificant increase of 1.1 ($P > 0.10$; 95% CI: −0.45 to 2.65) between baseline and postintervention follow-up and an increase of 3.3 ($P < 0.001$; 95% CI: 1.73–4.87) between baseline and long-term follow-up. The RAVLT showed a nonsignificant increase of 1.9 ($P < 0.10$; 95% CI: −0.32 to 4.13) between baseline and postintervention follow-up and an increase of 4.15 ($P < 0.001$; 95% CI: 1.87–6.43) between baseline and long-term follow-up. Semantic fluency also showed a time effect ($P = 0.02$ in Models 1 and 2) reflecting that a slight increase in score of 0.33 ($P > 0.4$; 95% CI: −0.58 to 1.24) between baseline and postintervention changed to a trend for a decrease of −0.82 ($P < 0.10$; 95% CI: −1.76 to 0.13) in words listed between baseline and long-term follow-up. These effects of time occurred in the absence of a group effect, meaning the effects over time followed a similar trajectory in all three groups for each test.

Secondary analyses

Previous research has shown that insulin resistance is associated with poorer cognitive outcomes and brain health (33-36). Insulin resistance was significantly improved in the CR groups in this study (14). Inclusion of change in HOMA-IR did not significantly alter the main effect of group but strengthened the effect of visit time point on the EF composite score ($P = 0.0435$; Table 4).

Because peak VO2 improved in all groups, we tested whether improved VO2 was associated with improved cognitive performance. Cognitive outcomes were tested using Model 2 adding change in peak VO2. No statistically significant associations were observed between change in peak VO2 and any cognitive outcomes (Table 4).

Sensitivity analyses

Although intervention compliance was excellent, individual variation existed in the amount of weight lost. Therefore, we tested whether the
amount of weight lost (rather than randomized group assignment) predicted cognitive outcomes. Percent weight loss following the intervention was added to Model 2 in place of group assignment. No statistically significant associations between percent weight loss and difference in group mean in any EF outcomes were observed. It appeared from the overall effect from mixed-effect models that weight loss was associated with a small improvement in MMSE score ($\beta = -0.06; P = 0.02$).

Achieving the same weight loss target (e.g., 5%) required a different absolute reduction in caloric intake in each person. In order to explore the possibility that the absolute amount of caloric reduction influenced cognition, the caloric reduction for each individual was used in Model 2 instead of group assignment. No statistically significant associations between calorie reduction and any EF outcome were observed. However, cutting more calories was associated with a slightly better MMSE score ($\beta = 0.002; P = 0.001$).

**Discussion**

Establishing the risks and benefits of intentional weight loss for adults over the age of 65 is currently an important research topic given the rapid aging of the population, increasing prevalence of obesity, and equipoise in the field. We tested whether addition of CR to a 20-week aerobic exercise intervention potentiated the short- and long-term benefits of exercise on EF. EF improved in the overall sample immediately post intervention; however, we did not observe statistically significant differences between groups in postintervention EF immediately or 18 to 24 months post intervention. Sensitivity analyses to test for effects of weight loss and absolute amount of calorie reduction independent of group did not alter outcomes.

A modest association was noted between group randomization and better global cognition measured with the MMSE based on Model 2.
| Outcome                  | Postintervention, adjusted mean (95% CI) | >Long-term follow-up, adjusted mean (95% CI) |
|--------------------------|------------------------------------------|---------------------------------------------|
|                          | Ex Only | Ex + Mod CR | Ex + High CR | Ex Only | Ex + Mod CR | Ex + High CR | P value, visit | P value, group |
| **Model 3**              |         |             |              |         |             |              |               |               |
| EF composite             | 0.178 (0.038 to 0.319)                  | 0.251 (0.124 to 0.378)                      | 0.158 (−0.025 to 0.256)                    | 0.359 (0.069 to 0.325)                     | 0.189 (0.060 to 0.317)                       | 0.0435 | 0.6445 |
| DSC                      | 44.29 (41.84 to 46.75)                  | 45.26 (43.06 to 47.46)                      | 46.21 (43.77 to 48.65)                     | 47.35 (45.10 to 49.59)                     | 47.18 (44.96 to 49.40)                       | 0.0038 | 0.7269 |
| Trials B-A               | 43.40 (31.59 to 55.20)                  | 46.33 (35.78 to 56.88)                      | 49.01 (37.32 to 60.70)                     | 51.94 (40.94 to 62.95)                     | 44.22 (33.55 to 54.88)                       | 0.1847 | 0.4346 |
| Stroop interference      | 27.16 (23.00 to 31.32)                  | 30.16 (26.35 to 33.97)                      | 28.58 (24.84 to 32.31)                     | 31.04 (27.31 to 34.77)                     | 29.89 (26.05 to 33.73)                       | 0.3338 | 0.5021 |
| Semantic fluency         | 20.59 (19.13 to 22.05)                  | 21.27 (19.93 to 22.61)                      | 21.27 (19.97 to 22.57)                     | 19.21 (17.75 to 20.66)                     | 19.89 (18.55 to 21.23)                       | 0.0058 | 0.6852 |
| Phonemic fluency         | 13.99 (12.81 to 15.17)                  | 12.97 (11.91 to 14.03)                      | 14.08 (12.90 to 15.26)                     | 13.06 (11.98 to 14.14)                     | 12.63 (11.57 to 13.69)                       | 0.7118 | 0.1260 |
| RAVLT                    | 49.11 (45.58 to 52.64)                  | 45.03 (41.74 to 48.31)                      | 46.94 (43.67 to 50.22)                     | 47.30 (43.95 to 50.65)                     | 49.22 (45.89 to 52.55)                       | 0.0121 | 0.2014 |
| MMSE                     | 27.66 (27.07 to 28.26)                  | 27.65 (27.08 to 28.22)                      | 28.25 (27.70 to 28.80)                     | 28.04 (27.45 to 28.64)                     | 28.03 (27.44 to 28.63)                       | 0.1093 | 0.0960 |
| **Model 4**              |         |             |              |         |             |              |               |               |
| EF composite             | 0.175 (0.041 to 0.308)                  | 0.119 (−0.003 to 0.242)                     | 0.146 (0.024 to 0.268)                     | 0.134 (0.001 to 0.267)                     | 0.079 (−0.047 to 0.205)                      | 0.105 (−0.018 to 0.229)                      | 0.1884 | 0.7943 |
| DSC                      | 44.45 (42.10 to 46.80)                  | 43.58 (41.48 to 45.69)                      | 43.67 (41.55 to 45.79)                     | 46.54 (44.21 to 48.87)                     | 45.67 (43.51 to 47.83)                       | 45.76 (43.60 to 47.91)                       | 0.0021 | 0.7834 |
| Trials B-A               | 43.70 (32.67 to 54.74)                  | 47.61 (37.72 to 57.51)                      | 40.18 (30.20 to 50.14)                     | 48.79 (37.94 to 59.64)                     | 52.70 (42.29 to 63.11)                       | 45.25 (34.94 to 55.55)                       | 0.2259 | 0.4650 |
| Stroop interference      | 27.33 (23.37 to 31.32)                  | 31.55 (27.95 to 35.14)                      | 28.63 (25.06 to 32.20)                     | 28.89 (24.97 to 32.81)                     | 33.11 (29.34 to 36.88)                       | 30.19 (26.50 to 33.88)                       | 0.2445 | 0.1801 |
| Semantic fluency         | 20.43 (19.13 to 21.73)                  | 20.49 (19.31 to 21.68)                      | 20.75 (19.56 to 21.94)                     | 19.36 (18.07 to 20.64)                     | 19.42 (18.18 to 20.66)                       | 19.68 (18.45 to 20.90)                       | 0.0241 | 0.8913 |
| Phonemic fluency         | 13.35 (12.23 to 14.46)                  | 12.69 (11.66 to 13.69)                      | 12.42 (11.42 to 13.43)                     | 13.48 (12.37 to 14.59)                     | 12.82 (11.79 to 13.84)                       | 12.55 (11.53 to 13.57)                       | 0.5991 | 0.3491 |
| RAVLT                    | 48.74 (45.51 to 51.96)                  | 44.11 (41.16 to 47.06)                      | 47.26 (44.26 to 50.25)                     | 50.86 (47.66 to 54.07)                     | 46.24 (43.20 to 49.29)                       | 49.39 (46.32 to 52.45)                       | 0.0177 | 0.0561 |
| MMSE                     | 27.64 (27.06 to 28.23)                  | 27.80 (27.27 to 28.34)                      | 28.38 (27.84 to 28.92)                     | 28.00 (27.42 to 28.58)                     | 28.16 (27.59 to 28.73)                       | 28.73 (28.17 to 29.30)                       | 0.1336 | 0.0533 |

Model 3 adjusted for Model 2 variables + HOMA2-IR change. Model 4 adjusted for Model 2 variables + peak VO2 change.
pants with type 2 diabetes who also had obesity at baseline (BMI ≥ 30), baseline BMI and long-term cognitive outcomes such that, in partici-

The Look AHEAD study observed a significant interaction between study, lifestyle changes were maintained > 1 year, and modest cogni-

The relatively short duration of interventions and duration of follow-up for these studies raise important points about how long an exercise intervention should last. In the current study, the EF composite score did not improve between short- and long-term follow-up. However, the DSC task and the RAVLT showed continued improvements in score at long-term follow-up. In the Napoli study(22), most cognitive outcomes did not improve between short- and long-term follow-up. However, the exercise-only group had no significant weight loss. They examined change in cognitive score at baseline, 6 months, and 12 months. After 12 months, both the exercise and exercise-plus-CR groups showed cognitive benefit compared with control. As here, they saw no significant differences between exercise and exercise plus CR. Therefore, it may be that exercise is the more potent inter-

The Look AHEAD study supports the idea that a longer lifestyle modi-

The Look AHEAD study observed a significant interaction between baseline BMI and long-term cognitive outcomes such that, in partici-

Conclusion

This study adds to accumulating evidence that adding intentional weight loss to exercise does not positively or negatively influence cogni-

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