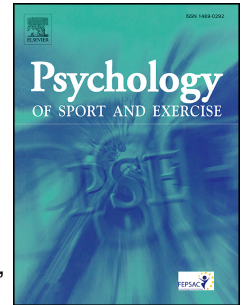


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Running head: COORDINATION EXERCISE, OBESITY, & COGNITION

A randomized controlled trial of coordination exercise on cognitive function in obese adolescents

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Results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

Running head: COORDINATION EXERCISE, OBESITY & COGNITION

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Abstract

Objective. Whether the beneficial effect of coordination exercise on executive function extends to obese adolescents remains understudied and no study to date has examined the effect of exercise on food-cue related executive function. The aim of this randomized controlled trial was to investigate the effects of a coordination exercise program on executive function in obese adolescents.

Design. A randomized controlled trial.

Methods. Eighty obese adolescents were randomly assigned to a 12-week coordination exercise program or a waitlist control group and data from 70 participants (n=35 for each group) were analyzed. The after-school exercise program involving a multifaceted moderate-intensity jump rope program performed twice weekly for 75 min per session. The primary outcome of normal and food-cue related Stroop task performance was assessed prior to and following the intervention. Secondary outcomes included physical fitness and body mass index (BMI).

Results. The coordination exercise intervention improved both normal and food-cue related cognitive function. Similar beneficial effects were also found for physical fitness and BMI. However, pre-to-post intervention change in physical fitness and BMI did not significantly mediate enhanced cognitive and executive function performance.

Conclusion. In obese adolescents, a coordination exercise intervention is an effective approach to improve multiple aspects of cognitive function while enhancing physical fitness and reducing obesity. These findings also suggest a possible role of cognitive inhibition in exercise-associated weight loss among obese adolescents.

Keywords: physical activity, cognitive control, inhibition, Stroop task, obesity

A randomized controlled trial of coordination exercise on cognitive function in obese adolescents

With the adoption of sedentary lifestyles and excess caloric consumption, the prevalence and severity of obesity during childhood and adolescence has risen substantially in less than a generation. Approximately 20.5% of adolescents aged 12 to 19 years are obese and over one third (34.5%) are considered overweight or obese in the United States (Ogden, Carroll, Kit, & Flegal, 2014). The obesity epidemic is also a global phenomenon, with increasing rates observed from 1980 to 2013 in both developed and developing countries (Ng et al., 2014). Obesity in youth and adolescence has been linked to numerous comorbidities and is recognized as a primary risk factor for morbidity and premature mortality during adulthood (Biro & Wien, 2010; Reilly & Kelly, 2011).

The adverse health consequences associated with obesity have also been extended to cognitive function. While obesity has been associated with impairments in multiple cognitive domains (e.g., memory, global functioning, and verbal abilities), deficits in executive function have been specifically reported in obese children and adolescents (Smith, Hay, Campbell, & Trollor, 2011). Executive function, involving inhibition, updating, and shifting (Miyake et al., 2000), refers to a higher or meta-level of cognitive processing that helps to guide, regulate, and optimize goal-directed behaviors, particularly in novel circumstances (Banich, 2009; Etnier & Chang, 2009). Elevated body mass index (BMI) has been inversely associated with executive processes of inhibition and switching (Cserjési, Luminet, Poncelet, & Lénárd, 2009; Cserjési, Molnár, Luminet, & Lénárd, 2007), and obese children were found to exhibit worse cognitive performance relative to their healthy weight counterparts in task conditions engaging inhibition (Kamiya et al., 2014).

The relationship between obesity and executive function is likely reciprocal, such that executive function (e.g., inhibition, updating) may help to regulate or prevent unhealthy

obesity-related behaviors in youth (Riggs, Huh, Chou, Spruijt-Metz, & Pentz, 2012; Riggs, Spruijt-Metz, Chou, & Pentz, 2012). For instance, compared to normal weight children, children with obesity demonstrated less activation in inhibition-related brain regions (e.g., prefrontal cortex) when responding to unhealthy food cues, suggesting that obese children may be at increased risk of food advertising and may have difficulty engaging healthy food decisions (Bruce et al., 2013). Indeed, attentional bias to food images has been associated with delayed inhibitory control (Braet & Crombez, 2003; Garcia-Garcia et al., 2013; Yokum, Ng, & Stice, 2011) and altered prefrontal cortex functioning (Garcia-Garcia et al., 2013; Yokum et al., 2011) among overweight and obese individuals. Obesity is a complex biological process that is influenced by factors at various levels of analysis (e.g., molecular/cellular, systems, behavioral [dietary intake, physical activity], and environmental; (Biro & Wien, 2010); however, recent findings relative to executive function suggest that inhibition or inhibitory control may serve as a potential neurobehavioral correlate or mechanism of obesity.

Existing and emerging cross-sectional evidence has consistently demonstrated that higher cardiorespiratory fitness is associated with greater executive function, particularly in inhibition, during childhood and adolescence (Pontifex et al., 2011; Pontifex, Scudder, Drollette, & Hillman, 2012; Wu et al., 2011). Recently, the FITKids randomized trial demonstrated that an afterschool physical activity program not only reduced total and central adiposity and improved cardiovascular fitness (Khan et al., 2014), but also enhanced the inhibitory domain of executive function as reflected by behavioral and neurophysiological (i.e., event-related potential) evidence (Hillman et al., 2014). Importantly, these beneficial effects were disproportionately larger for the inhibition-related task and a potential dose-response relation was found between change in physical fitness and improvement in inhibition, suggesting a causal influence of exercise and physical fitness on this component of

executive function. Furthermore, exercise has been observed to improve the efficiency and connectivity of multiple brain regions, including the anterior cingulate and prefrontal cortices (Voss et al., 2010), which are critically involved in inhibition. Nonetheless, these previous studies were limited to aerobic fitness and to a cardiovascular fitness-based physical activity program for children. Given that relationships between other components of physical fitness (e.g. muscular fitness, body composition, coordination) and cognition have recently been proposed in children with ADHD (Chang, Hung, Huang, Hatfield, & Hung, 2014; Hung et al., 2013) and among older adults (Niemann, Godde, & Voelcker-Rehage, 2014; Voelcker-Rehage, Godde, & Staudinger, 2010), it is possible that these exercise and fitness-related associations may extend to obese adolescents. Adolescence represents a critical transitional stage of physical and psychological development that generally occurs during the period from puberty to legal adulthood, and may be a particularly important developmental stage to implement evidence-based behavioral interventions.

Despite the emerging associations between exercise, physical fitness, obesity, and cognitive function, it remains unknown whether the beneficial effect of exercise on inhibition extends to adolescents with obesity. This is important, given the potential for a ‘critical window’ during adolescence to address obesity and instill healthy eating behaviors. Improving executive function in general, and inhibition in particular, may help strengthen positive behavioral choices as well as restraint to more unhealthy options. For instance, exercise-induced improvements in executive-function were recently found to mediate improvements in dietary self-restraint on a subsequent laboratory taste test involving high-calorie snack foods (Lowe, Koley, & Hall, 2016). Given that the few available randomized controlled trials (RCTs) of exercise on cognition in youth have relied on aerobic forms of exercise, RCTs incorporating other components of physical fitness are warranted. Moreover, no study to date has explored the effect of exercise on food-cue related inhibitory

control, even though suggestions towards health-related self-regulatory behaviors have been suggested (Hofmann, Schmeichel, & Baddeley, 2012).

Therefore, the aim of this RCT was to evaluate the effects of a novel, multi-faceted exercise program on cognition and food-cue related inhibition as well as physical fitness and BMI in obese adolescents. A secondary exploratory aim was to determine whether pre-to-post intervention changes in cognition and food-cue related inhibition were mediated by changes in physical fitness and BMI. We predicted that a coordination-based exercise program would improve cognition and food-cue related inhibition, as well as physical fitness and BMI. Furthermore, it was hypothesized that improved physical fitness and BMI would mediate enhanced normal and food-cue related cognitive performance.

Methods

Study Design

A 12-week RCT design was used to investigate the cognitive effects of a coordination exercise program in adolescents with obesity. The length of the trial was determined based on a previous meta-analysis suggesting a positive effect of chronic exercise on cognitive function in children (Sibley & Etnier, 2003) and a previous RCT of aerobic exercise for overweight children (Davis et al., 2007). Twelve weeks has also been suggested as a minimum duration for school-based interventions to prevent childhood obesity (Brown & Summerbell, 2009). The primary outcome of this trial was cognitive function and inhibitory control assessed through Stroop task (including the modified food-related Stroop task); Secondary outcomes included physical fitness and BMI as well as additional cognitive function measures (i.e., Tower of London task). Considering the primary outcome and purpose of the trial was focused on inhibition and food-cue related inhibitory control, only cognitive performance data from the Stroop task is presented herein. A trained experimenter masked to group allocation administered the primary and secondary outcome measures.

Participants, Screening, and Allocation

Ninth to eleventh grade adolescents were recruited from a junior high school in New Taipei City, Taiwan. Eligibility criteria included: a) ages 12 to 16 years; b) obesity with a body mass index (BMI) $> 24 \text{ kg/m}^2$; c) ability to safely engage in exercise as determined by the physical activity readiness questionnaire (PAR-Q); d) normal intelligence (Taiwan Junior High School Intelligence Examination (TJHSIE) > 90). (Note: excellence > 120 , outstanding = 90-100, low = 70-89); e) normal or correct-to-normal vision without color-blindness; f) free from a history of brain injuries or psychiatric disorders; and g) a score of < 1500 metabolic equivalents/week on the International Physical Activity Questionnaire (IPAQ). After baseline assessments, 80 eligible participants stratified by gender were randomly allocated using a pseudorandom computer-generated algorithm to either a coordination exercise group or to waitlist control group for 12-weeks. Allocation was performed and participants were informed about group allocation by a research assistant who was not involved in the pre- and post-intervention assessments or the coordination exercise training. Seventy participants ($n=35$ for each group) completed both pre- and post-assessments, and were included in the analysis. The number of included participants is similar to previous trials of exercise and obesity in children (Davis et al., 2007), although may be low for reliable statistical estimates within the context of previous meta-analytic evidence of exercise and cognition (Sibley & Etnier, 2003). A CONSORT study flow diagram is presented in Figure 1. All participants and their parents or guardian provided written informed assent/consent prior to participation in the study, which was approved by a government-referred Institutional Review Board.

Outcome Measures

Cognitive Function. As a primary outcome, a modified version of the classic Stroop color-word conflict task that assesses multiple aspects of cognitive function and has demonstrated sensitivity to exercise interventions (Chang, Tsai, Huang, Wang, & Chu, 2014)

was employed. The stimuli were three color word names presented in Chinese as 藍 (BLUE)、紅 (RED)、綠 (GREEN), and colored rectangles. The Stroop task is comprised of three congruency conditions: a) in the congruent condition the meaning of the word matches the color ink (e.g., the word BLUE is presented in blue ink); b) in the color condition a rectangle is presented in one of the ink colors; and c) in the incongruent condition the meaning of the word and color of the ink conflict (e.g., the word BLUE is presented in red ink). To examine obesity-related executive function, we created an additional food cue-related Stroop task condition (i.e., food-cue condition). In this condition, stimuli were three different food cues: 漢堡 (Burger), 炸雞 (fried chicken), and 薯條 (French fries) presented in one of the ink colors. The Stroop task was administered in the same order both at baseline (pre-test) and following the 12-week intervention (post-test, i.e., congruent, color, incongruent, and food cue-related task conditions).

Each of the four conditions consisted of 50 stimuli randomly presented on a sheet of paper. Following verbal instructions, participants were presented with the stimuli and asked to identify and verbally name the color ink of each stimulus from top to bottom (10 stimuli) and left to right (5 columns) as quickly and accurately as possible. Once an error occurred, a trained experimenter administering the task informed the participant that an error had occurred, and to verbally name the color ink again. The main outcome measure was response time(s) across each block of the Stroop task, which was assessed using stopwatch by a trained experimenter masked to treatment allocation.

Physical Fitness. As a secondary outcome, physical fitness was assessed using a nationally based test battery designed specifically for school-aged students that is administered by the Ministry of Education (MOE) in Taiwan. The fitness test battery assesses four components of physical fitness: cardiovascular fitness was determined based on time to completion during a 1600 m (male) or 800 m (female) run/walk test; muscular endurance and

flexibility were determined through a one-min sit-up test and a sit-and-reach test, respectively. Lastly, anaerobic power was quantified as the distance performed in a standing long jump. All fitness tests were conducted and supervised by a qualified and certified instructor, and participants were encouraged provide maximal effort for each test.

Obesity. As a secondary outcome, body composition was assessed using BMI, computed as weight in kg divided by height in m². BMI has frequently been used as an indirect measure of obesity in children and adolescents (Cole, Faith, Pietrobelli, & Heo, 2005).

Testing Procedures. Each participant completed the outcome measures in each test session (pre-and-post intervention) in the following order: cognitive function testing, BMI-assessment, and the physical fitness test battery. Each testing session was conducted in a specific classroom within the school. Given the logistical constraints of conducting a RCT within a school setting, including recruiting participants from different classes and conducting the measures individually, all outcome measures were conducted within a week prior to and following the intervention, respectively.

Exercise Intervention

The exercise intervention was a novel after-school jump rope program designed to address both cardiovascular and coordinative components of physical fitness. The modified program (Davis et al., 2011; Gutin, Riggs, Ferguson, & Owens, 1999) was proposed to reduce BMI and enhance children's physical fitness. The 12-week exercise program consisted of two sessions/week for 75 min/session, and each session started and ended with an 8 min warm up (brisk walking) and cool down (slow walking, static stretching), as well as two 20 min bouts of the main jump rope exercise with a 5-10 min rest interval between the two exercise bouts. The jump rope exercise program emphasized intensity (maintaining HR at approximately 150-170 bpm), fun, and safety rather than competition. Participants wore Polar HR monitors (S610i; Polar Electro, Oy, Finland) during exercise and were encouraged to maintain their

target HR throughout sessions. Participants who engaged above or below 150-170 bpm were instructed to decrease or increase intensity to maintain the moderate intensity of exercise. The exercise instructor was a physical educator with a MS degree in exercise physiology and was jump rope certified. The student-teacher ratio across the program administration was 9 to 1.

Statistical Analysis

Statistical analyses were performed by a researcher masked to group allocation by labelling the groups with nonidentifying terms. A sample size calculation was performed with G*Power version 3.1 (Faul, Erdfelder, Lang, & Buchner, 2007) based on the assumption of a medium to large effect size in favor of coordination exercise in obese adolescents ($\alpha = .05$; $1 - \beta = 0.8$). We used a medium to large effect size (Cohen's $f = 0.35$) for our trial considering small effects for exercise on cognition observed among youth in general (Sibley & Etnier, 2003), and larger effects found for the inhibition domain of executive function among obese children (Reinert & Barkin, 2013), and for the Stroop task relative to other executive function measures (Brush, Olson, Ehmann, Osovsky, & Alderman, 2016). This indicated that approximately 33 participants per group (~67 total participants) were needed to detect significant effects. The trial was not powered for BMI or fitness-related secondary outcomes. However, collection of these data enabled assessment of feasibility of this data collection relative to a coordinative exercise program in adolescents, and the provision of effect size estimates to inform sample size for subsequent trials. Descriptive statistics were initially performed on participant demographic, physical fitness, and cognitive data.

The Stroop task data, including findings from the Stroop food-cue task condition, were analyzed using analyses of covariance (ANCOVA) because methodological studies suggest that controlling for baseline scores is advantageous relative to conventional pre-post comparisons or analyses using change scores (Vickers & Altman, 2001). This analytical approach also increases statistical power relative to pre-test/post-test designs, and accounts

for baseline differences and potential for regression to the mean. Specifically, we used ANCOVA to examine differences in post-test scores of reaction time measures for the Stroop trials by group (coordination exercise, waitlist control) controlling for pre-test scores (de Boer, Waterlander, Kuijper, Steenhuis, & Twisk, 2015). In addition, ANCOVA was used to explore possible changes in the four physical fitness measures (i.e., cardiovascular fitness, muscular fitness, flexibility, and power) and BMI from pre-to-post intervention, while controlling for baseline values. The analyses were identical using both a per-protocol and an intention-to-treat (ITT) strategy, and the per-protocol analysis is presented considering all participants with post-intervention data. Significance tests were conducted with a family-wise alpha level set at .05 and effect sizes are presented as partial eta-square (η_p^2).

Finally, bivariate correlations were conducted to examine relationships between change in physical fitness, BMI, and cognition. Exploratory mediation analyses were also conducted to further explore these relationships. The separate mediation models postulated that the coordination exercise intervention would predict the mediating variable, i.e. change physical fitness and BMI, which in turn would predict enhanced normal and food-cue related Stroop task performance at post-intervention, while controlling for baseline values (Fairchild & MacKinnon, 2014). For the mediation analyses, change scores for all four fitness variables and BMI were z-scored and collapsed into a single physical fitness variable. Mediation analyses were conducted using PROCESS software for SPSS (v2.15; Hayes, 2013) using 5000 resamples and bias corrected bootstrapped 95% confidence intervals. For all analyses, regression was conducted for path a (predictor \rightarrow mediator), path b (mediator \rightarrow outcome), path c (predictor \rightarrow outcome), and path c' (true indirect effect). Statistical significance of the mediation was achieved if the estimated 95% confidence interval for the indirect effect (paths c-c') did not include zero.

Results

Participant Demographics

Table 1 summarizes participants' demographic characteristics. Both the coordination exercise group and the control group were comparable with respect to demographics, fitness, and cognitive performance at baseline. Although testing for baseline differences in pre-test/post-test designs has been argued to serve little purpose and may potentially be misleading (de Boer et al., 2015), these data confirm the groups were comparable at baseline.

Cognitive Function Assessment

Table 2 presents the results of the ANCOVA models for the Stroop cognitive outcomes as well as physical fitness and BMI variables by group, controlling for baseline scores. For the Stroop task analysis, group comparisons showed that coordination exercise group improved performance on all Stroop task conditions at follow-up relative to the waitlist control group ($ps < 0.001$, η_p^2 values ≥ 0.33) (Figure 2a). Relative to the Stroop food-cue condition, the ANCOVA analyses revealed faster response times at follow-up for the coordination exercise relative to waitlist control group, $p < .001$, $\eta_p^2 = .33$, Figure 2b).

Physical Fitness

ANCOVA analyses revealed significant group differences among cardiovascular fitness, suggesting a shorter time-to-completion at post-test compared to pre-test for the coordination exercise group ($p < 0.001$, $\eta_p^2 = 0.50$; see Table 2, Figure 3a). Similarly, the analysis for muscular fitness revealed significantly more sit-up repetitions at post-test compared to pre-test for the coordination exercise group, $p < 0.001$, $\eta_p^2 = 0.49$. Analyses for flexibility ($\eta_p^2 = 0.30$) and anaerobic power ($\eta_p^2 = 0.55$) also revealed significant group differences at follow-up, $ps < 0.001$.

Obesity (BMI) Assessment

Group differences were observed for BMI at follow-up, with the coordination exercise group having a lower BMI than the control group, $p < .001$, $\eta_p^2 = 0.58$. BMI was

nonsignificantly higher at post-intervention compared to baseline for the control group, $p = 0.16$, Table 2, Figure 3b.

Bivariate Correlation and Mediation Analyses

Cardiovascular fitness was significantly associated with indices of the Stroop task ($r_s = 0.31$ to 0.51 , $p_s < 0.001$), with greater pre-to-post increase in cardiovascular fitness associated with greater positive change in cognitive performance (Table 3). A similar correlation pattern was also observed between other indices of physical fitness (muscular fitness, flexibility, and power) and cognition indices (Figure 4a). BMI was also significantly associated with Stroop task performance ($r_s = 0.46$ to 0.68 , $p_s < 0.001$), with greater pre-to-post change in BMI associated with more positive change in cognitive performance (see Figure 4b). The exploratory mediation analysis using changes in physical fitness (and BMI) from pre-to-post intervention demonstrated nonsignificant paths a and b and significant paths c and c' for all Stroop outcome measures. The c coefficient represents the total effect and suggests a significant overall effect of coordination exercise on the cognitive performance outcomes. The significant c' coefficient represents the direct effect and demonstrates an effect of the coordination exercise program on the Stroop task outcomes while controlling for the mediating variable (change in physical fitness). However, the true indirect effect for the model ($c - c'$) of the treatment intervention enhancing cognitive performance outcomes through change physical fitness was not significant for Stroop Congruent ($\beta = -0.08$, 95% CI $(-0.76, 0.06)$), Incongruent ($\beta = -0.13$, 95% CI $(-1.00, 0.19)$), Color ($\beta = -0.10$, 95% CI $(-0.56, 0.07)$), or the food-cue related inhibition ($\beta = -0.10$, 95% CI $(-1.13, 0.43)$) tasks.

Discussion

In this RCT, we tested the effect of a novel 12-week coordinative exercise-training program for improving cognition and the inhibition component of executive function in a

sample of obese adolescents. A secondary aim was to determine whether physical fitness and BMI improve following the intervention, and whether changes in these physical health outcomes mediate intervention-related improvements in cognitive function. We also aimed to advance the literature by examining food-cue related inhibition using an adapted Stroop task paradigm. Relative to the waitlist control group, the coordination exercise group showed an improvement in multiple aspects of cognitive performance. That is, adolescents assigned to the 12-week coordination exercise program outperformed participants randomized to the waitlist control in all conditions of the Stroop task following the intervention, including the food-cue related inhibitory control task condition. Notably, obese adolescents who participated in the coordination exercise program also significantly improved in a number of physical fitness indices reflecting aerobic fitness, muscular fitness, flexibility, and anaerobic power, as well as demonstrated a reduction in BMI relative to adolescents assigned to the waitlist comparison group. Although the treatment-related improvement of physical fitness and BMI outcomes were positively associated with enhanced Stroop task performance, these physical health outcomes did not significantly mediate change in cognitive performance outcomes in exploratory mediation analyses. Thus, the findings suggest that a novel 12-week coordinative exercise program results in improved physical health outcomes and improvements in executive function and inhibitory control cognitive processes in obese adolescents. We believe these findings provide a promising foundation for future research to examine alternative modes of exercise to improve cognitive function, as well as interventions aimed at younger cohorts who may be at a critical stage of development and who are at risk of early unhealthy behaviors (e.g., inactivity, unhealthy eating).

In accordance with the results of previous cardiovascular and aerobic exercise intervention studies, (Davis et al., 2011; Hillman et al., 2014; Pontifex et al., 2011; Pontifex et al., 2012; Wu et al., 2011), enhanced cognitive performance was observed following the

12-week coordination exercise intervention. The improved cognitive function performance observed from pre-to-post intervention in our study is slightly larger (Cohen's d values ranged from 0.56 to 0.60) than findings from a previous study (Hillman et al., 2014; $d = 0.27$ to 0.34), but is within the range of effects reported in the Sibley and Etnier (2003) meta-analysis ($ds = 0.00$ to 1.49). The larger improvement found in this study might be associated with the nature of the intervention. Compared to previous studies that involved daily physical education or low-intensity walking, our intervention resulted in maintenance of a moderate level of exercise intensity across exercise sessions. Importantly, the coordination exercise group also exhibited enhanced performance on the food-cue related task condition of Stroop task. These findings suggest that a coordinative exercise program may be effective at impacting inhibitory control brain regions that have previously been implicated in obesity. That is, obese versus normal weight individuals have been shown to exhibit greater attentional bias and reward-associated brain network activation to high-fat/calorie food images (Yokum et al., 2011), but less activation in prefrontal regions responsible for the inhibition component of executive function (Stice, Spoor, Bohon, Veldhuizen, & Small, 2008). Kamijo et al., 2014 observed that overweight children selectively recruit lower prefrontal neural resources during an inhibitory control task, suggesting that obese children may experience deficits in inhibition to food cues. Our findings demonstrated enhanced cognitive performance following 12 weeks of coordination exercise, and extend these cognitive benefits to food-cue related inhibition. Although speculative, these findings suggest that facilitation of food-cue related inhibition following the coordination exercise intervention may play a role in the improved physical fitness and decreased BMI measures in obese adolescents. However, it should be noted that testing associations of change scores across the intervention does not necessarily imply that changes in fitness and BMI serve as mediators of the improved cognitive outcomes following the coordination exercise intervention. And

indeed, changes in these physical health outcomes did not mediate the improvements in cognition and inhibition found at post-intervention in the coordinative exercise group. Future studies similarly incorporating regression-based statistical mediation analyses (Hayes & Rockwood, 2016) in RCT designs are warranted to determine whether changes in key fitness or physiological variables serve to mediate treatment-related improvements in cognitive function, with a particular focus on the inclusion of larger sample sizes of participants at known risk for cognitive decline (e.g., obese individuals). Plausible mediators proposed to explain the exercise and cognition relationship include changes in cardiorespiratory fitness (assessed through indirect calorimetry), cerebral blood flow, and brain neurotransmitters and neurotrophic factors implicated in neuronal proliferation and survival, including brain-derived neurotrophic factor.

Novel to our study was demonstrating for the first time that the consistent beneficial effects of exercise interventions on cognitive function extend to obese adolescents. Notably, while improved performances were observed for three conditions of Stroop task, participants assigned to the coordination exercise group exhibited larger enhancement on the Stroop incongruent condition that required more extensive inhibitory control compared to Stroop color and Stroop congruent conditions that represent basic information processing, suggesting that the coordination exercise not only had a general facilitation effect on different cognitive functions, but was more pronounced for executive function. This disproportionately greater effect for executive function is in line with previous studies that have applied other executive function tasks (e.g., flanker task; Hillman et al., 2014; Pontifex et al., 2011) and may be attributed to mental and brain resources responsive to cardiovascular fitness. That is, neurophysiological (i.e., event-related potential) and neuroimaging studies indicate that higher-fit children elicit a greater amount of neural resources (Hillman et al., 2014; Pontifex

et al., 2011) and more efficient neural processing (Chaddock et al., 2012; Voss et al., 2011) during executive function tasks relative to their lower-fit counterparts.

In terms of mechanisms, the multifaceted coordination exercise program might share similar mechanisms for improving cognition relative to more traditional cardiovascular fitness based exercise. Chang, Tsai, Chen, and Hung (2013) observed that eight-weeks of an alternative coordination exercise intervention (i.e., soccer) not only facilitated performance on a flanker task among 5-6 year-old children, but also resulted in an increased allocation of attentional resources during task completion. Similarly, neural processes in older adults may also be influenced by the type of exercise engaged in, with several studies demonstrating cardiovascular and motor physical fitness (e.g., flexibility, motor coordination) were associated with greater activation in sensorimotor and visual-spatial networks, respectively (Niemann et al., 2014; Voelcker-Rehage et al., 2010; Voelcker-Rehage, Godde, & Staudinger, 2011). Whether different types of exercise programs result in enhanced cognition through diverse mechanisms and associated alterations in brain and cognitive functions requires further investigation. It is also possible that individual differences in exercise preference may interact with traditional psychobiological mechanisms suggested to underlie the cognitive-enhancing benefits of exercise. The role of exercise preference in the cognitive enhancing benefits of exercise warrants future research attention.

Another noteworthy finding in this study was the effects of the coordinative exercise program on physical health outcomes. The effects of the coordination exercise program on cardiovascular fitness and BMI outcomes were similar to previous trial of aerobic exercise (Hillman et al., 2014; Khan et al., 2014); however, our jump rope exercise program involved moderate-to-vigorous exercise intensity with a visual-motor skill component and bilateral coordination (Miyaguchi, Sugiura, & Demura, 2014) that collectively would likely lead to additional physical fitness benefits. Furthermore, the magnitude of BMI reduction following

this novel, coordination exercise intervention is both statistically and clinically meaningful. Specifically, the coordination exercise program resulted in a moderate to large magnitude of reduction in BMI (Cohen's $d = 0.71$). The larger change might be associated with various aspects of intervention (e.g., novelty) and the associated motivation of the participants. Compared to previous studies that involved in daily physical education or walking, the current intervention provided participants with a new and stimulating experience that many considered fun and motivating. In addition, given the obesity status of the participants, many may have had higher motivation to change their physique. Taken together, this coordination exercise program may be an effective treatment program for physical fitness improvements and weight control in obese adolescents.

There are several strengths and limitations of our study. This is the first randomized trial assessing coordination exercise in obese adolescents, emphasizing an effect of a multi-faceted exercise program on diverse cognitive functions and specifically on the food cue-related executive function task. However, our relatively short intervention (12 weeks) may be insufficient to reflect clinically meaningful change in physical fitness, weight control, and cognitive function, and thus longer interventions are encouraged in future studies. Nevertheless, we found significant effects of the coordination exercise intervention on these diverse outcomes relative to both baseline and to a waitlist comparison control group. The degree of change was in line with previous studies in children (Chang et al., 2013; Davis et al., 2011; Hillman et al., 2014; Khan et al., 2014).

A critical issue in RCT design is the choice of primary versus secondary outcomes and the clear and transparent reporting of trial methodology and findings (Schulz, Altman, & Moher, 2010). Given the findings from the FITKids trial demonstrating an effect of an afterschool physical activity program on cardiovascular fitness, adiposity, and inhibitory control (Hillman et al., 2014), we selected the Stroop task (including the food-related Stroop

inhibition task) as our primary outcome. We also powered our trial using a medium to large effect size given that larger effects have been reported for the inhibition domain of executive function in obese children (Reinert & Barkin, 2013), as well as the improved sensitivity for the Stroop task relative to other executive function measures (Brush et al., 2016). However, it is possible that the trial was not sufficiently powered, especially for the mediation analyses. Given the time and resources available to complete the study, we could only recruit ~40 participants per group. After dropouts and discontinuation, this left a total of 70 participants in total for tests of our hypotheses on cognition and food-cue related inhibition as well as the exploratory mediation of physical fitness and BMI. A larger sample size would have increased the precision of our estimates of the effect of the coordination exercise program on these outcomes. It is thus critical for future studies to recruit sufficient sample sizes and use appropriate methods for randomized behavioral interventions to advance this area of research. Furthermore, future studies with larger sample sizes should test for potential mediators of cognitive outcomes following exercise interventions. Our findings herein suggest that changes in physical performance and BMI health outcomes, at least using standardized field-based approaches, may not have the requisite sensitivity to serve as plausible mediators of the exercise-cognitive function relationship. Lastly, without including multiple points and a follow-up period, it is unclear whether these short-term benefits are sustainable. However, the results extend previous correlational research and suggestions about coordination-based exercise routines (Diamond & Lee, 2011) and provide a robust preliminary test that warrants further study in overweight and obese school-age populations.

Conclusion

The multifaceted coordination exercise program was effective at enhancing both general and food-related executive function and improving physical fitness and reducing BMI among obese adolescents. However, the intervention-related changes in physical fitness did

not significantly mediate the improved cognitive outcomes observed following the coordination exercise intervention, suggesting the need for trials with larger sample sizes or examination of alternative mediators of these relationships. Nonetheless, the current study extends the pediatric literature on obesity, cognitive function, and exercise, particularly during the potential critical developmental period of adolescence, and points to the need for implementing evidence-based public health interventions for overweight and obese adolescents.

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The authors declare no conflict of interest.

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Table 1. Participants' baseline demographic characteristics (mean \pm SD).

| Variables | Coordination Exercise (n = 35) | Waitlist Control (n = 35) |
|--------------------------------------|-----------------------------------|------------------------------|
| Age (year) | 13.94 \pm 0.94 | 14.17 \pm 0.71 |
| males/females (%) | 20/15 (42.86%) | 20/15 (42.86%) |
| Height (cm) | 162.45 \pm 5.73 | 164.40 \pm 8.32 |
| Weight (kg) | 74.33 \pm 12.16 | 75.86 \pm 13.95 |
| Body mass index (kg/m ²) | 28.01 \pm 3.03 | 27.92 \pm 3.29 |
| Intelligence Quotient (TJHSIE) | 96.11 \pm 3.04 | 96.43 \pm 2.87 |
| Education (yrs) | | |
| Father | 14.00 \pm 3.01 | 14.57 \pm 2.80 |
| Mother | 14.60 \pm 2.99 | 14.46 \pm 2.94 |
| Family income | | |
| < NT 20,000 | 8.57% | 8.57% |
| NT 20,000 to 40,000 | 20% | 17.14% |
| NT 40,000 to 60,000 | 20% | 22.86% |
| NT 60,000 to 80,000 | 31.43% | 25.71% |
| > NT 80,000 | 20% | 25.71% |
| Resting heart rate (bpm) | 91.86 \pm 12.49 | 95.66 \pm 11.26 |
| IPAQ (MET min/week) | | |
| Baseline | 916.00 \pm 105.09 | 913.80 \pm 96.18 |
| After intervention | 1713.14 \pm 105.05* | 923.17 \pm 123.50 |

Note. TJHSIE = Taiwan Junior High School Intelligence Examination; NT = New Taiwan Dollar; IPAQ = International Physical Activity Questionnaire; METs = Metabolic equivalents.

* $p < .05$

Table 2. Group differences across time for cognitive function, physical fitness and obesity variables (mean \pm SD)

| Variable | Coordination Exercise (<i>n</i> = 35) | | Waitlist Control (<i>n</i> = 35) | | ANCOVA | |
|--------------------------|---|---------------------|--------------------------------------|---------------------|----------|-----------------|
| | Pre-test | Post-test | Pre-test | Post-test | <i>F</i> | <i>p</i> -value |
| Stroop task | | | | | | |
| Congruent (sec.) | 21.08 \pm 5.27 | 18.43 \pm 3.33 | 20.55 \pm 4.42 | 20.51 \pm 4.38 | 32.97 | .00 |
| Color (sec.) | 28.47 \pm 6.29 | 24.94 \pm 5.67 | 28.04 \pm 4.84 | 28.55 \pm 7.22 | 57.23 | .00 |
| Incongruent (sec.) | 45.50 \pm 9.85 | 40.38 \pm 8.39 | 51.38 \pm 15.04 | 54.22 \pm 14.97 | 64.00 | .00 |
| Food-cue (sec.) | 39.63 \pm 8.92 | 30.92 \pm 6.52 | 37.47 \pm 10.95 | 37.78 \pm 10.05 | 33.77 | .00 |
| Physical fitness | | | | | | |
| Cardio. (sec.) | 552.40 \pm 247.83 | 506.97 \pm 235.50 | 579.71 \pm 260.93 | 634.97 \pm 295.10 | 65.93 | .00 |
| Muscular Fitness (rep.) | 29.71 \pm 7.43 | 32.17 \pm 7.30 | 28.20 \pm 8.11 | 26.29 \pm 7.67 | 63.86 | .00 |
| Flexibility (cm) | 28.77 \pm 10.18 | 29.91 \pm 9.90 | 28.82 \pm 9.97 | 28.25 \pm 9.88 | 28.51 | .00 |
| Power (cm) | 146.63 \pm 25.28 | 160.99 \pm 21.45 | 145.12 \pm 28.41 | 142.73 \pm 27.87 | 81.53 | .00 |
| BMI (kg/m ²) | 28.01 \pm 3.03 | 25.99 \pm 2.67 | 27.92 \pm 3.29 | 28.16 \pm 3.34 | 93.92 | .00 |

Note. Cardio = Cardiovascular fitness; BMI = Body mass index; rep. = repetitions.

Table 3. Bivariate correlation matrix for difference scores for physical fitness, BMI and cognition outcomes.

| Measure | Cardiovascular fitness | Muscle fitness | Flexibility | Power | BMI |
|-------------|------------------------|----------------|-------------|--------|-------|
| Stroop task | | | | | . |
| Congruent | .31** | -.31** | -.24* | -.36** | .46** |
| Color | .51** | -.53** | -.36** | -.40** | .59** |
| Incongruent | .48** | -.58** | -.46** | -.46** | .68** |
| Food-cue | .39** | -.35** | -.30** | -.26* | .47** |

* $p < .05$; ** $p < .001$, BMI = Body mass index.

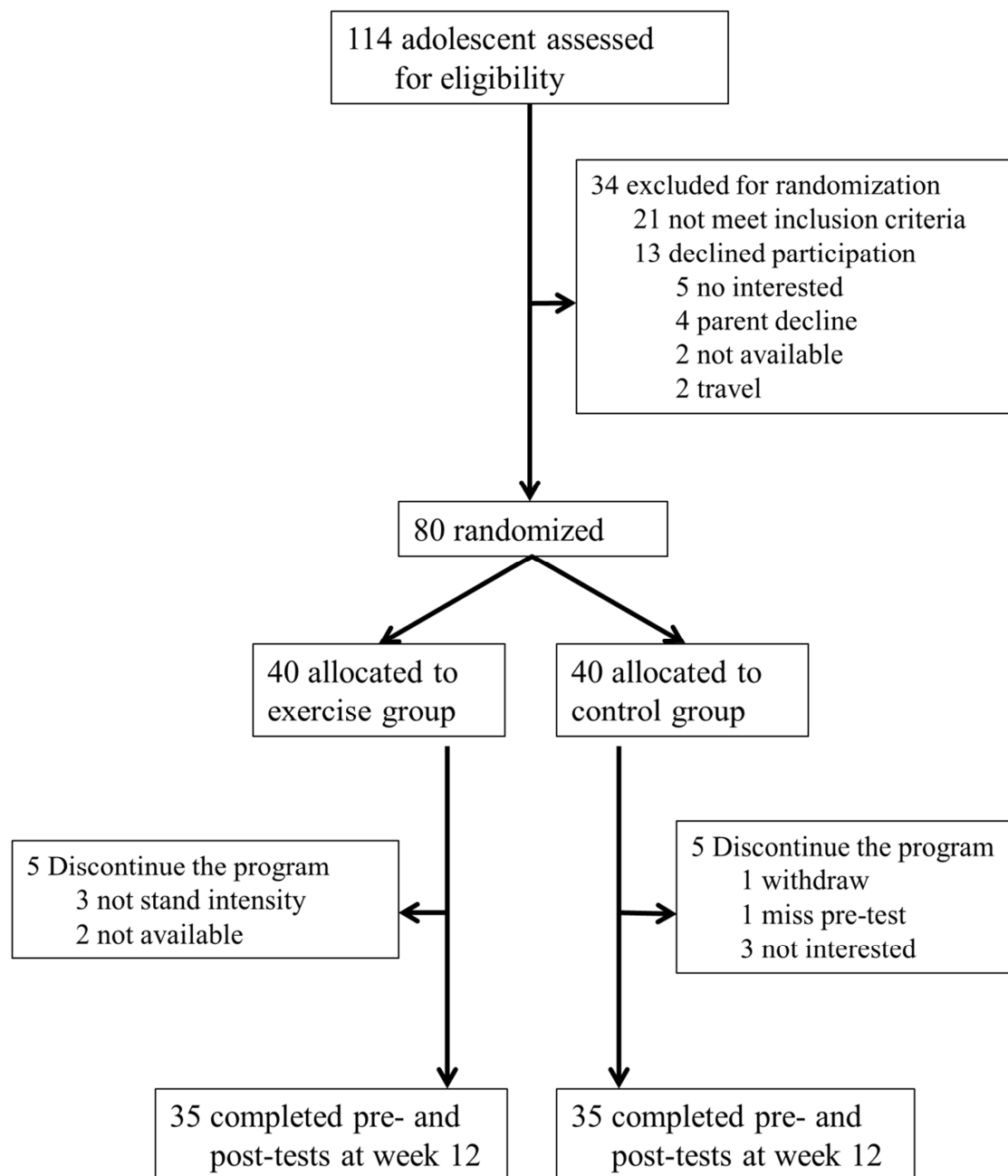


Figure 1. CONSORT study diagram for recruitment, allocation, and intervention.

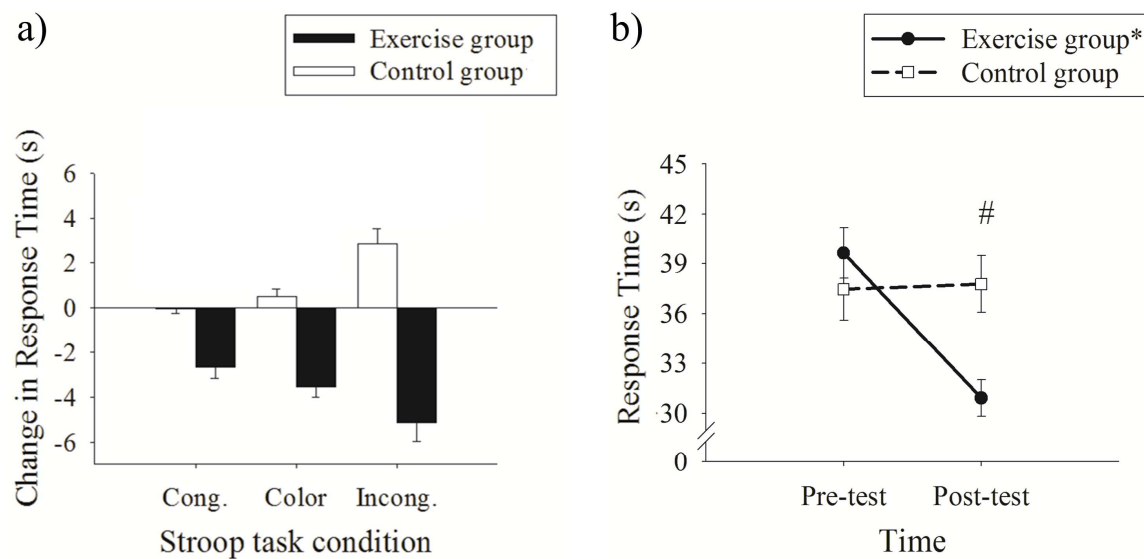


Figure 2. a) Difference scores of response time at follow-up minus baseline values across groups and three Stroop task conditions; and b) response time of Stroop food cue-related condition as a function of group and time (pre and post-intervention). Lower response times represent better performance. For figure b), *represents a significant difference within condition, # represents a significant difference between groups.

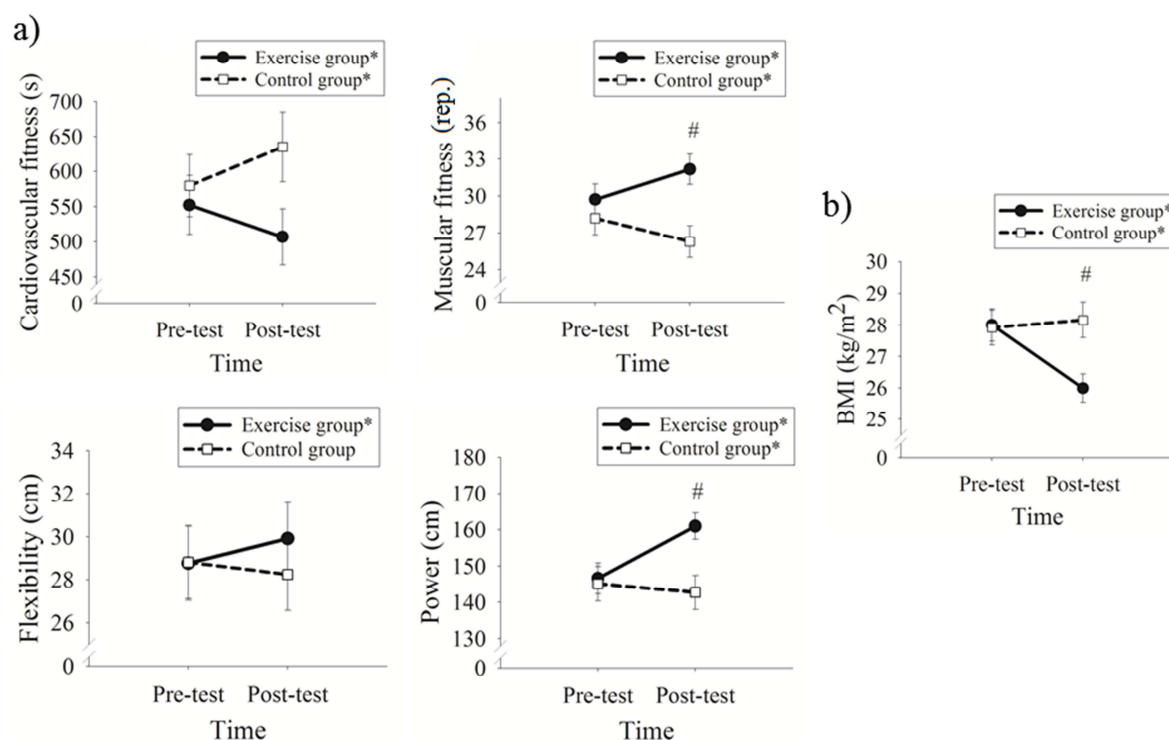


Figure 3. Physical fitness and obesity outcomes as function of group and time (pre- and post-intervention). *represents a significant difference within condition, # represents a significant difference between groups.

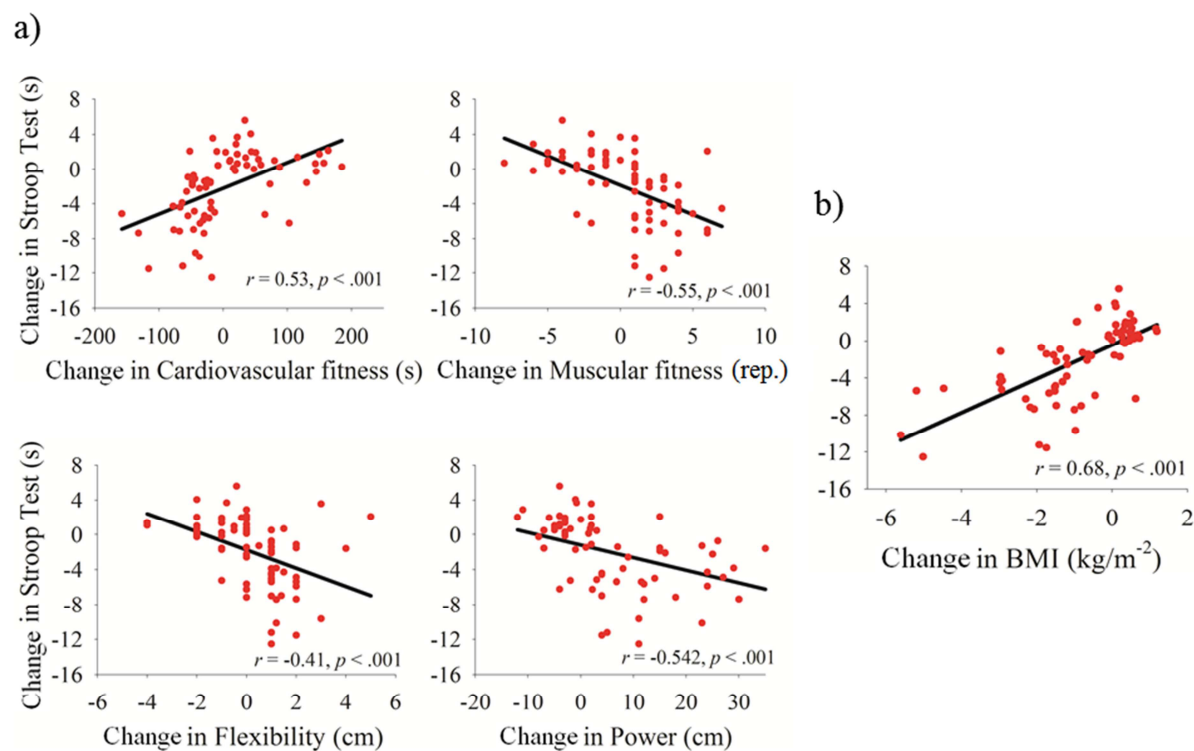


Figure 4. Scatter plots demonstrating significant correlations between change scores in outcomes of a) physical fitness and Stroop task performance; and b) BMI and Stroop task performance.

1 Highlight

- 2 ● Effect of the coordination exercise on executive function in obese adolescent remains
3 understudied
- 4 ● The multifaceted coordination exercise program was effective at improving physical
5 fitness and reducing obesity.
- 6 ● The program also benefits to enhance both general and obesity-related executive
7 function among obese adolescents.
- 8 ● There is a possible role of obesity-related inhibition in exercise-associated weight loss
9 among obese adolescents.