

V. THE DIFFERENTIAL ASSOCIATION OF ADIPOSITY AND FITNESS WITH COGNITIVE CONTROL IN PREADOLESCENT CHILDREN

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ABSTRACT With the increasing prevalence of sedentary behaviors during childhood, a greater understanding of the extent to which excess adiposity and aerobic fitness relate to cognitive health is of increasing importance. To date, however, the vast majority of research in this area has focused on adiposity or fitness, rather than the possible inter-relationship, as it relates to cognition. Accordingly, this study examined the differential associations between body composition, aerobic fitness, and cognitive control in a sample of 204 (96 female) preadolescent children. Participants completed a modified flanker task (i.e., inhibition) and a switch task (i.e., cognitive flexibility) to assess two aspects of cognitive control. Findings from this study indicate that fitness and adiposity appear to be separable factors as they relate to cognitive control, given that the interaction of fitness and adiposity was observed to be nonsignificant for both the flanker and switch tasks. Fitness exhibited an independent association with both inhibition and cognitive flexibility whereas adiposity exhibited an independent association only with cognitive flexibility. These results suggest that while childhood obesity and fitness appear to both be related to cognitive control, they may be differentially associated with its component processes.

Epidemiological investigations within industrialized societies have revealed increases in both the prevalence of sedentary behaviors and the incidence of metabolic-related diseases (e.g., cardiovascular disease, colon cancer, and type-2 diabetes; DHHS and DOE, 2000). Thus, the discordant nature of our current lifestyle relative to our physiological predisposition toward activity may be disadvantageous for both our physical and cognitive health (Booth &

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Lees, 2006; Hillman, Erickson, & Kramer, 2008; Vaynman & Gomez-Pinilla, 2006). Beyond the body of literature demonstrating a positive association between physical activity and cognitive health, a growing number of investigations have begun to suggest that a healthy body composition may also be important for the optimal developmental trajectory of brain maturation and cognitive development. Recent findings have indicated a negative association between weight status and scholastic achievement (Datar & Sturm, 2006), with a number of longitudinal studies indicating that school-based interventions designed to promote appropriate weight gain during development can improve academic achievement (Donnelly et al., 2009; Hollar, Lombardo et al., 2010; Hollar, Messiah et al., 2010).

However, to better understand the relationship between body composition and cognition, an important consideration may be the level of cognitive load imposed by a given task. That is, using data from the Third National Health and Nutrition Examination Survey conducted between 1988 and 1994, Li, Dai, Jackson, and Zhang (2008) observed that higher BMI in children aged 8–16 years was associated with poorer visual-spatial organization and working memory. Alternatively, Gunstad et al. (2008) failed to observe a relationship between BMI and cognitive performance on tests of motor function, verbal recall, attention, and memory in a similarly aged sample. These apparently discrepant findings may be rectified by consideration of the extent to which the differential tasks used in these investigations necessitated aspects of higher-order cognition. Consonant with such an assertion, a more robust relationship between weight status and cognition has been observed for task components requiring aspects of cognitive control relative to other aspects of cognition (Cserjési, Molnár, Luminet, & Lénárd, 2007; Kamijo, Pontifex et al., 2014; Li et al., 2008; Lokken, Boeka, Austin, Gunstad, & Harmon, 2009).

As described in Chapter 3, the term cognitive control (also referred to as “executive control”) describes a subset of cognitive operations, which encompass the selection, scheduling, coordination, and maintenance of computational processes underlying perception, memory, and action (Rogers & Monsell, 1995). The core cognitive processes that collectively comprise cognitive control include inhibition (the ability to resist distraction or habits to maintain focus), working memory (the ability to actively store, maintain, and manipulate information to be retrieved within a brief interval), and cognitive flexibility (the ability to dynamically shift attention, select information, and alter response strategy in response to changing task demands; Barkley, 1997; Davidson, Amso, Anderson, & Diamond, 2006; Kane & Engle, 2002; Postle, 2006). These goal directed processes allow for the optimization of behavioral interactions within the environment through the flexible modulation of attentional control (Botvinick, Braver, Barch, Carter, & Cohen, 2001; MacDonald, Cohen, Stenger, & Carter, 2000). This ability to adapt to varying demands is often considered to be a hallmark of human

intelligence and is increasingly utilized over the course of development as children acquire knowledge, develop routines, and master tasks and skills in increasingly varied environmental settings (Deák, 2004; Spensley & Taylor, 1999). Accordingly, findings have suggested a negative association between childhood obesity and components of cognitive control; including inhibition (Kamijo, Kahn, et al., 2012; Kamijo, Pontifex, et al., 2012), working memory (Li et al., 2008), and cognitive flexibility (Cserjési et al., 2007; Lokken et al., 2009). Further, findings from a number of recent neuroimaging studies have indicated negative associations between BMI and gray matter volume in neural areas subserving aspects of cognitive control in adult populations (Maayan, Hoogendoorn, Sweat, & Convit, 2011; Raji et al., 2010).

Interestingly, lower-levels of aerobic fitness have also been previously found to be associated with decreased cognitive performance across a variety of tasks, with a selectively greater deficit for aspects of cognitive control (Chaddock, Hillman et al., 2012; Hillman, Buck, Themanson, Pontifex, & Castelli, 2009; Kamijo et al., 2011; Pontifex et al., 2011; but see Hillman et al., 2008 for review). A few prior investigations on the relationship between adiposity and cognition have controlled for the relation of fitness within their analysis; yet given the remarkable similarity between the relationship of aerobic fitness and obesity to cognitive control—and the inherent relationship between aerobic fitness and obesity—the question still remains open regarding how distinct these bodies of literature actually are. That is, both obesity and aerobic fitness can be conceived as attributes resulting from the engagement in healthy lifestyle behaviors and complex interactions of genetics and environmental factors. Thus, to date we have little understanding of how these two bodies of literature may be more broadly reflecting a similar continuum of healthy behaviors, or how they might interact to influence cognitive health and function.

The purpose of this investigation was to determine the individual and combined contributions of aerobic fitness and adiposity on two aspects of cognitive control; inhibition and cognitive flexibility. Although the vast majority of research investigating the relationship between weight status and cognition has utilized BMI as a surrogate measure of adiposity; in order to quantify adiposity as accurately as possible, dual-energy X-ray absorptiometry (DXA) was used to provide measures of whole body adiposity and fat-free mass. Similarly, aerobic fitness is traditionally corrected for body size using total body mass; however, within this investigation we corrected based only on fat-free mass to have two separable measures of fitness and adiposity. Thus, although fitness and adiposity are highly interrelated constructs, this approach allows for the dissociation of these factors to the fullest extent possible using presently available techniques. Based upon previous research, which has repeatedly demonstrated that aerobic fitness attenuates the risk of metabolic disease associated with excess adiposity (Barlow, Kohl, Gibbons, &

Blair, 1995; Church et al., 2004; Lee, Blair, & Jackson, 1999; Lee et al., 2005), it was hypothesized that aerobic fitness would interact with adiposity, such that greater amounts of adiposity would only be negatively related to tasks requiring extensive amounts of inhibitory control and cognitive flexibility for individuals with poorer cardiorespiratory fitness.

METHOD

The methodology for this study involved a sample of 252 (116 female) preadolescent children, who were recruited from the east central Illinois area as part of a larger ongoing longitudinal study investigating the effects of aerobic fitness on cognitive control. Participants were excluded if they did not participate in either the aerobic fitness, body composition, or cognitive assessments ($N = 34$) or if they were unable to perform the cognitive tasks at a minimum 40% correct threshold (i.e., they correctly answered fewer than 60 trials out of the 150 trials of the Flanker or Switch tasks [Moore et al., 2013; Rueda, Rothbart, McCandliss, Saccomanno, & Posner, 2005]; $N = 14$). Analyses were conducted on the remaining sample of 204 participants (106 White or Caucasian, 45 Black or African American, 26 Asian, 27 bi-racial or of other ethnicities, with 13 identified as being of Hispanic origin; see Table 1 for descriptive characteristics). All participants provided written assent and their

TABLE 1
PARTICIPANT DEMOGRAPHIC VALUES (± 1 SD)

Measure	All Participants
<i>N</i>	204 (96 female)
Age (years)	8.8 \pm .6 (range: 7.7–10.0)
Tanner stage	1.4 \pm .5 (range: 1–3)
Maternal Education	3.9 \pm 1.0 (range: 1–5)
K-BIT composite (IQ)	111.0 \pm 13.8 (range: 86–145)
Body mass index (kg/m ²)	19.2 \pm 4.4 (range: 13.0–37.4)
Body mass index percentile	67.9 \pm 29.0 (range: 1–99)
Whole body fat (kg)	11.1 \pm 6.5 (range: 2.9–33.1)
Whole body percent fat (%)	28.0 \pm 8.2 (range: 12.1–45.8)
VO ₂ max (ml/kg/min)	38.2 \pm 7.1 (range: 19.9–53.2)
VO ₂ max percentile	19.7 \pm 21.8 (range: 3–85)
VO ₂ max_FFM (ml/kg of FFM/min)	52.7 \pm 7.0 (range: 28.8–67.1)

Note. Maternal Education—educational attainment was quantified on a scale from 1 indicating that they did not complete high-school to five indicating earning an advanced degree. K-BIT—standardized score of intelligence quotient from the Kaufman Brief Intelligence Test (Kaufman & Kaufman, 1990). Body mass index percentile—based on normative values for body mass index (Kuczmarski et al., 2002). VO₂max Percentile—based on normative values for VO₂max (Shvartz & Reibold, 1990). VO₂max_FFM—maximal oxygen consumption corrected for fat-free body mass.

legal guardians provided written informed consent in accordance with the Institutional Review Board of the University of Illinois at Urbana-Champaign. Prior to testing, legal guardians completed a health history and demographics questionnaire, reported that their child was free of neurological diseases or physical disabilities, and indicated (corrected to) normal vision.

The participants performed several tasks to assess aspects of cognitive control. To assess inhibition, we measured behavioral indices of performance during a modified version of the Eriksen flanker task (Eriksen & Eriksen, 1974). This task is conceptually simplistic in that it requires the discrimination of a centrally presented target stimulus amid lateral flanking target stimuli (see Figure 1). In this task, participants were required to make a left hand thumb press on a Neuroscan STIM system response pad (Compumedics, Charlotte, NC) when the target stimulus pointed left and a right hand thumb press when the target stimulus pointed right. Thus, participants were instructed to respond as accurately as possible to the direction of a centrally presented target goldfish amid either congruous (facing the same direction) or incongruous (the target faces the opposite direction) flanking goldfish stimuli. After completing 40 practice trials, participants completed two blocks of 75 trials presented with equiprobable congruency and directionality. The

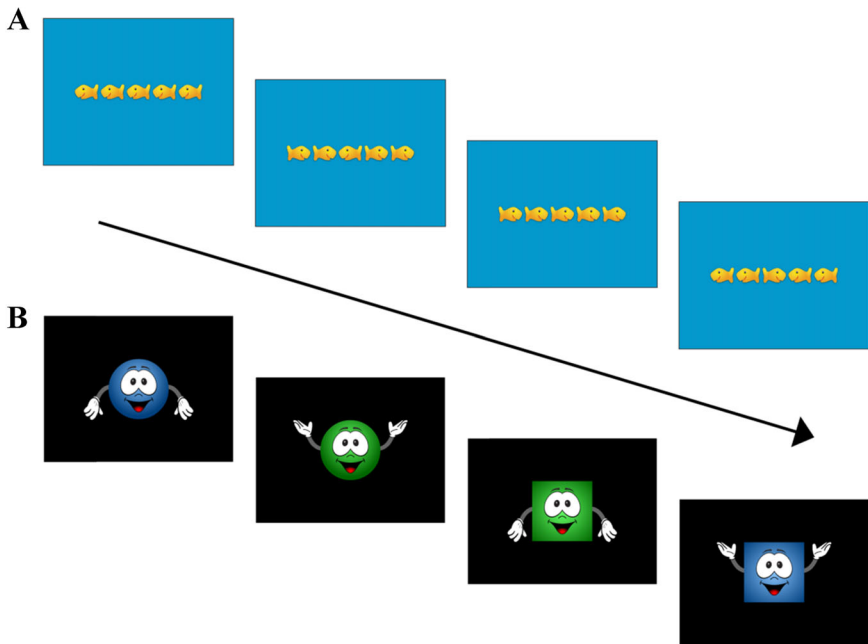


FIGURE 1.—Illustration of the flanker task (A) and heterogeneous switch task (B).

stimuli were 3 cm tall yellow goldfish, which were presented focally for 200 ms on a blue background with a fixed inter-trial interval of 1,700 ms.

To assess aspects of cognitive flexibility, we measured behavioral indices of performance during a color-shape switch task (Espy, 1997). Participants viewed circle and square shaped characters presented in either blue or green with their arms up or down (see Figure 1). This task requires participants to learn a set of response mappings arbitrarily assigned to a set of colors (blue and green) and shapes (circle and square), and then utilize a rule-set cue (the direction of the characters arms) to flexibly shift visuospatial attention toward the correct feature set and execute the correct response mapping. In this task, participants completed two blocks of 60 homogeneous trials (1 block of color only; 1 block of shape only) in which they attended to a centrally presented character. Participants were instructed to make a left hand thumb press on a Neuroscan STIM system response pad (Compumedics) when the character was blue (in the color condition) or a circle (in the shape condition) and a right hand thumb press when the character was green (in the color condition) or a square (in the shape condition). During the heterogeneous condition, participants performed both the color and shape tasks together with the specific task on each trial indicated by the direction of the character's arms (arms up: respond based on the shape of the character; arms down: respond based on the color of the character). After completing 40 practice trials, participants completed three blocks of 50 heterogeneous trials with equiprobable task occurrence and response directionality. The stimuli were 5.5 cm tall, 9 cm wide, characters presented focally for 3,000 ms on a black background, or until a response was given, with a fixed inter-trial interval of 3,500 ms.

In addition to cognitive assessments, we measured various aspects of health and fitness. Specifically, body composition was assessed using standing height and weight measurements with participants wearing lightweight clothing and no shoes. Height and weight were measured using a Tanita WB-300 Plus digital scale (Tanita Corp, Tokyo, Japan). DXA was utilized to measure whole body composition (providing measures of fat and fat-free mass) using a Hologic Discovery A bone densitometer (software version 12.7.3; Hologic, Inc., Bedford, MA). Precision for DXA measurements of interest are ~1–1.5% in our laboratory.

Further, aerobic fitness was assessed using a test of maximal oxygen consumption (VO_2max), which describes the physiological limit to the rate at which an individual can deliver/consume oxygen and is considered the criterion measure of cardiorespiratory fitness (American College of Sports Medicine, 2006). Maximal oxygen consumption was measured using a computerized indirect calorimetry system (ParvoMedics True Max 2400, Sandy, UT) with averages for VO_2 and respiratory exchange ratio (RER) assessed every 20 s. A modified Balke protocol (American College of Sports

Medicine, 2006) was employed using a motor-driven treadmill at a constant speed with increases in grade increments of 2.5% every 2 min until volitional exhaustion occurred. A Polar heart rate monitor (Polar WearLink+ 31; Polar Electro, Finland) was used to measure heart rate throughout the test and ratings of perceived exertion were assessed every 2 min using the children's OMNI scale (Utter, Robertson, Nieman, & Kang, 2002). Attainment of VO₂max was qualified based upon maximal effort as evidenced by either (1) a peak heart rate > 185 bpm (American College of Sports Medicine, 2006) and a heart rate plateau corresponding to an increase of less than 5 bpm despite an increase in workload (Freedson & Goodman, 1993); (2) RER > 1.0 (Bar-Or, 1983); (3) a score on the children's OMNI ratings of perceived exertion scale > 7 (Utter et al., 2002); and/or (4) a plateau in oxygen consumption corresponding to an increase of less than 2 ml/kg/min despite an increase in workload. Approximately 89% of the participants attained 2 or more of the specified criteria. In order to reduce the colinearity between whole body adiposity and aerobic fitness measures, maximal oxygen consumption was corrected relative to fat free mass (ml/kg of FFM/min). Such an approach is considered to have greater validity than maximal oxygen consumption relative to total body weight (ml/kg/min) when comparing aerobic fitness in children of different body sizes (Goran, Fields, Hunter, Herd, & Weinsier 2000).

The procedures used to collect the various cognitive and physical assessments occurred over several laboratory visits. On the first visit to the laboratory, participants completed an informed assent and the Kaufman Brief Intelligence Test (K-BIT; Kaufman & Kaufman, 1990) to assess IQ. Concurrently, participants' legal guardians completed an informed consent, health history and demographics questionnaire, a modified Tanner Staging System questionnaire to assess pubertal status, and the Physical Activity Readiness Questionnaire (Thomas, Reading, & Shephard, 1992) to screen for any previous health issues that might be exacerbated by exercise. Maternal educational attainment—quantified on a scale from 1 indicating that they did not complete high school to 5 indicating earning an advanced degree—was used as a proxy for socioeconomic status. After completing all questionnaires, being fitted with a Polar heart rate monitor (Polar WearLink[®]+ 31, Polar Electro), and having their height and weight measured, participants completed a maximal exercise test on a motorized treadmill to assess aerobic fitness. On the second visit, participants performed cognitive testing while seated in a sound attenuated room. Following the provision of task instructions, participants were afforded the opportunity to ask questions and practice the task prior to the start of testing. Upon completion of the last task condition, a DXA measurement was performed to assess body composition.

Statistical analysis was performed using several approaches. Bivariate correlation analyses were conducted using Pearson product-moment correlation coefficients between demographic factors and cognitive control

domains. Hierarchical linear regression analyses were then performed to examine variance in performance across cognitive control domains as they related to three separate models. Models 1 and 2 characterized the independent contribution of aerobic fitness (as assessed using VO_2max corrected for fat-free mass; model 1: $Y = \alpha + \beta_1\text{aerobic fitness} + B'\text{demographic factors}$) and adiposity (as assessed using whole body total fat mass; model 2: $Y = \alpha + \beta_2\text{adiposity} + B'\text{demographic factors}$), respectfully, for explaining the variance beyond that of statistically significant descriptive correlates (Age, Sex, Tanner Stage, Mothers Education, IQ, and Race). Model 3 then characterized the additive effects of both aerobic fitness and adiposity for explaining variance in performance within each cognitive control domain (model 3: $Y = \alpha + \beta_1\text{aerobic fitness} + \beta_2\text{adiposity} + \beta_3\text{aerobic fitness} \times \text{adiposity} + B'\text{demographic factors}$). The interaction of fitness and adiposity was observed to be nonsignificant for all variables of interest, $\Delta R^2\text{'s} \leq .01$, $p\text{'s} \geq .14$, $f^2 \leq .01$. Similarly, no significant associations were observed between fitness and adiposity for RT for either the flanker or switch tasks ($r \leq |.10|$, $p \geq .17$), thus only findings for response accuracy are reported. A form of sensitivity analysis was also conducted to quantify how large the impact of an omitted variable must be to invalidate the observed inferences (Frank, 2000); defining impact as $r_{yv} \times r_{xv}$: the product of the correlation (r_{yv}) between the confounding variable and the outcome (cognitive control domain), and the correlation (r_{xv}) between the confounding variable and the predictor of interest (adiposity and fitness). Thus, the impact threshold for a confounding variable (ITCV) specifies how strongly a confounding variable must be related to both the outcome and the predictor of interest (controlling for any other related factors) to abrogate the observed effect. Across all analytical procedures, α was set at .05 with the specific significance level of each relationship denoted in Tables 2 and 3. Cohen's f^2 is provided as a standardized measure of effect size. All data analyses were performed in PASW Statistics, 19.0 (IBM, Somers, NY).

RESULTS

The statistical analysis resulted in several interesting findings relative to fitness and body mass. Specifically, results of the correlational and regression analysis for behavioral performance in response to the flanker task are provided in Tables 2 and 3, respectively. The hierarchical regression analysis indicated that Age and IQ explained a statistically significant amount of variance for both congruent ($F(2,201) = 9.49$, $p < .001$, $f^2 = .09$, $\beta_{\text{Age}} = .25$, $\beta_{\text{IQ}} = .18$) and incongruent ($F(2,201) = 7.99$, $p < .001$, $f^2 = .08$, $\beta_{\text{Age}} = .23$, $\beta_{\text{IQ}} = .16$) response accuracy. Beyond the variance accounted for by these demographic factors, all three models exhibited similar findings with aerobic fitness ($\Delta F\text{'s}(2,199) \geq 5.68$, $p\text{'s} \leq .004$, $f^2 \geq .05$) serving to explain a statistically

TABLE 2
BIVARIATE CORRELATIONS BETWEEN DEMOGRAPHIC FACTORS AND NEUROCOGNITIVE DOMAINS

Variable	Fitness	Adiposity	Age	Sex	Tanner	M. Education	K-BIT IQ	Race	F. Cong.	F. Inco.	S. Homo.	S. Hetero.
Fitness	—											
Adiposity	-.34**	—										
Age	.06	.22**	—									
Sex	.15*	-.27**	-.05	—								
Tanner	-.18**	.22**	.21**	.04	—							
M. Education	.27**	-.20**	.00	.01	-.12	—						
K-BIT IQ	.18**	-.07	-.09	-.02	-.08	.32**	—					
Race	-.22**	.14*	.05	.10	.10	-.11	-.25**	—				
F. Cong.	.25**	.04	.23**	-.09	-.09	.06	.16*	.02	—			
F. Inco.	.23**	.10	.22**	-.12	-.01	.03	.14*	.02	.83**	—		
S. Homo.	.11	-.11	.16*	-.16*	.02	.10	.09	.07	.27**	.31**	—	
S. Hetero.	.22**	-.10	.22**	-.08	-.08	.19**	.17*	.15*	.22**	.20**	.39**	—

Note: Fitness—maximal oxygen consumption corrected for fat-free body mass. Adiposity—whole body total fat. Sex—dummy coded as 0 = Female, 1 = Male. Race—dummy coded as 0 = White, 1 = Non-white. M. Education—mother's educational attainment. F. Cong.—response accuracy for the congruent trials of the flanker task. F. Inco.—response accuracy for the incongruent trials of the flanker task. S. Homo.—response accuracy for the homogenous trials of the switch task. S. Hetero.—response accuracy for the heterogeneous trials of the switch task.

* $p \leq .05$.

** $p \leq .01$.

TABLE 3
SUMMARY OF HIERARCHICAL REGRESSION ANALYSES

	R^2	R^2 Change ^a	B	$SE\ B$	β	t	VIF	ITCV
Congruent response accuracy								
Model 1: VO ₂ max_FFM	.13	.04**	.37	.12	.21	3.16**	1.04	.092
Model 2: Whole body total fat	.09	.00	-.01	.13	.00	.04	1.05	
Model 3	.14	.05**						
VO ₂ max_FFM			.43	.13	.24	3.37**	1.19	.107
Whole body total fat			.16	.14	.09	1.17	1.21	
Incongruent response accuracy								
Model 1: VO ₂ max_FFM	.11	.04**	.33	.11	.20	2.93**	1.04	.075
Model 2: Whole body total fat	.08	.00	.11	.13	.06	.84	1.05	
Model 3	.13	.06**						
VO ₂ max_FFM			.42	.12	.25	3.49**	1.19	.117
Whole body total fat			.27	.13	.15	2.10*	1.21	.010
Heterogeneous response accuracy								
Model 1: VO ₂ max_FFM	.18	.04**	.37	.13	.20	2.90**	1.13	.072
Model 2: Whole body total fat	.16	.02*	-.30	.14	-.15	2.14*	1.12	.012
Model 3	.19	.04**						
VO ₂ max_FFM			.31	.13	.17	2.34*	1.26	.028
Whole body total fat			-.19	.15	-.09	1.32	1.24	

Note. * $p \leq .05$,

** $p \leq .01$.

Model 1 assessed aerobic fitness, Model 2 assessed adiposity, and Model 3 assessed both aerobic fitness and adiposity.

VIF, variance inflation factor; ITCV, impact threshold for a confounding variable.

^aRelative to model of demographic factors. Models for Congruent and Incongruent Response Accuracy included Age and K-BIT composite (IQ). Models for Heterogeneous Response Accuracy included Age, Mothers Education, K-BIT composite (IQ), and Race.

significant and incremental amount of variance in congruent (β 's $\geq .20$, t 's (199) ≥ 3.16 , p 's $\leq .002$) and incongruent (β 's $\geq .2$, t 's (199) ≥ 2.93 , p 's $\leq .004$; see Figure 2) response accuracy. However, model 3, which assessed both aerobic fitness and adiposity, also observed an independent association between adiposity and incongruent response accuracy ($\beta = .15$, t (199) = 2.1, $p = .04$).

The results of the correlational and regression analysis for behavioral performance in response to the switch task are provided in Tables 2 and 3, respectively. The hierarchical regression analysis indicated that Age and Sex explained a statistically significant amount of variance for homogenous response accuracy (F (2,201) = 4.92, $p = .008$, $f^2 = .05$, $\beta_{\text{Age}} = .15$, $\beta_{\text{Sex}} = -.15$). However, neither adiposity nor aerobic fitness explained a statistically significant increase in variance in homogeneous response accuracy (ΔF 's (2,199) ≤ 3.51 , p 's $\geq .06$, $f^2 \geq .02$). For heterogeneous trials, hierarchical regression analysis indicated that Age, Mothers Education, IQ, and Race explained a statistically significant amount of variance in response accuracy (F

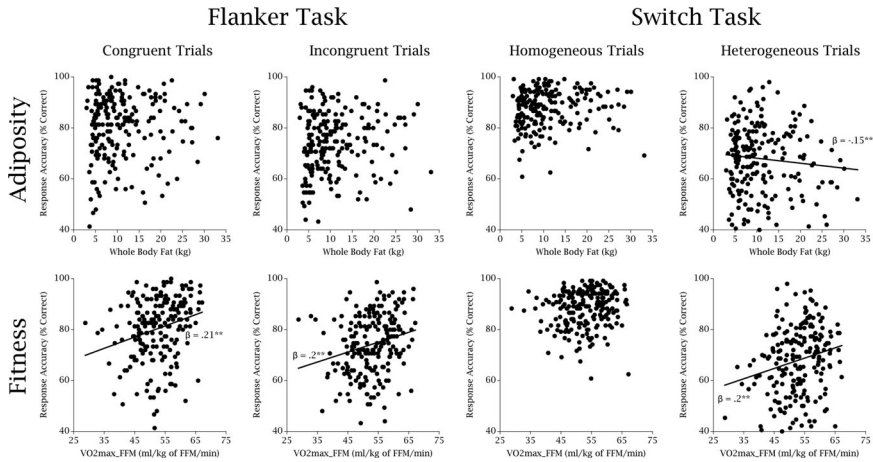


FIGURE 2.—Scatterplots of the relation between response accuracy, adiposity (top), and aerobic fitness (bottom) in response to the flanker task (left panels) and switch task (right panels). * $p \leq .05$, ** $p \leq .01$.

(4,199) = 8.33, $p < .001$, $f^2 = .17$, $\beta_{\text{Age}} = .23$, $\beta_{\text{Mothers Education}} = .15$, $\beta_{\text{IQ}} = .2$, $\beta_{\text{Race}} = .21$). Beyond the variance accounted for by these demographic factors, both aerobic fitness ($\Delta F(1, 198) = 8.38$, $p = .004$, $f^2 = .04$) and adiposity ($\Delta F(1, 198) = 4.57$, $p = .007$, $f^2 = .02$) served to explain a statistically significant and incremental amount of variance in heterogeneous response accuracy (see Figure 2). Model 3, which examined an additive model of adiposity and aerobic fitness observed that the independent contribution of adiposity did not reach statistical significance ($\beta = -.09$, $t(197) = 1.3$, $p = .19$).

DISCUSSION

This investigation was conducted to provide new insight into the specific relations of adiposity and aerobic fitness on two different aspects of cognitive control (i.e., inhibition and cognitive flexibility). Findings revealed an association between aerobic fitness and inhibition—with lower levels of aerobic fitness relating to poorer response accuracy for both congruent and incongruent trials of the flanker task; and cognitive flexibility with lower levels of aerobic fitness relating to poorer response accuracy for the heterogeneous condition of the switch task. Similarly, an association between adiposity and cognitive flexibility was observed with higher levels of adiposity relating to poorer response accuracy for the heterogeneous condition of the switch task. However, an association between adiposity and inhibition was only observed

for incongruent response accuracy when the variance associated with fitness was controlled. Contrary to our initial hypothesis, adiposity and fitness appear to be separable factors related to cognitive control as the interaction of adiposity and fitness was observed to be nonsignificant for all variables of interest. Thus, these results suggest that whereas childhood obesity and fitness are both related to cognitive control, they appear to be differentially associated with its component processes.

These findings corroborate previous research investigating fitness-related differences in cognitive control during childhood, which have examined bimodal higher- and lower-fitness groups (above the 70th percentile relative to below the 30th percentile based on age- and sex-based normative values), with lower levels of aerobic fitness relating to poorer behavioral performance for tasks requiring inhibitory control and cognitive flexibility (Chaddock, Hillman et al., 2012; Hillman et al., 2009; Pontifex et al., 2011). Novel to the present investigation is the extension of these findings in children to a continuum of fitness levels suggesting a linear relationship between aerobic fitness and these aspects of cognitive control. Such findings replicate previous research in adult populations demonstrating a small but significant effect of chronic physical activity behaviors leading to increased aerobic fitness on cognition (Etnier, Salazar, Landers, & Petruzzello, 1997). It should be noted, that the mean percentile rank of aerobic fitness using age- and sex-based normative values provided by Shvartz and Reibold (1990) for this sample was in the 19.6th percentile, suggesting that this sample constitutes a largely low-aerobic fitness population relative to the population norms. Although these data do not allow for speculation with regard to the extent to which this sample truly represents a lower-fit population cohort or if societal trends over the past several decades may be skewing population-wide aerobic fitness levels toward being lower-fit (see Chapter 2), the range of aerobic fitness levels in this investigation was normally distributed. Clearly, further research is necessary to examine the relationship between aerobic fitness and cognitive control across a more diverse representation of aerobic fitness to determine the extent to which this relationship is truly linear across the spectrum of fitness or if there is some threshold at which the cognitive benefits of increases in aerobic fitness taper off.

The present findings also replicate the extant literature relative to the relationship between body composition and cognitive control processes. Specifically, consistent with previous findings (Cserjési et al., 2007; Lokken et al., 2009), adiposity was negatively related to cognitive flexibility with higher levels of adiposity relating to poorer performance on the heterogeneous trials of the switch task. No such relationship was observed for the homogenous trials. The finding that adiposity was negatively related to performance on incongruent trials of the flanker task only after accounting for the variance associated with aerobic fitness replicate findings observed by Kamijo, Pontifex

et al. (2012) who first matched individuals across differing body composition levels based on sex and aerobic fitness prior to assessing the relationship between inhibition and body composition. Despite the negative relationship between adiposity and cognitive control processes observed within the present investigation, these findings should be interpreted with caution as we do not yet have an understanding of the causal direction of the association between adiposity and cognition. That is, Graziano, Calkins, and Keane (2010) observed that poorer inhibitory control in 2-year-old children is predictive of weight control problems 3.5 years later. Similarly, findings have revealed that gray matter volume in neural areas associated with cognitive control is predictive of weight gain over the following year in a female adolescent population (Yokum, Ng, & Stice, 2012). Conversely, enhanced scholastic achievement, which has been found to necessitate cognitive control processes (Bull & Scerif, 2001; DeStefano & LeFevre, 2004; St. Clair-Thompson & Gathercole, 2006), has been observed following school-based interventions specifically targeting weight gain during development (see Chapter 7; Donnelly et al., 2009; Hollar, Lombardo, et al., 2010; Hollar, Messiah, et al., 2010). Accordingly, further research utilizing longitudinal randomized control interventions is necessary to determine how changes in adiposity might influence cognitive control during development. Although speculative at this point, it may be that weight status and cognitive control constitute a feedback loop such that poorer control results in increased adiposity, which further impairs cognitive control. Despite such speculation, it is clear that an important factor for understanding the relationship between weight status and cognition is consideration of the aspect of cognition assessed.

Despite prior research indicating an interaction between adiposity and aerobic fitness for metabolic health, the present findings suggest that with regard to cognitive control, adiposity and fitness appear to be separable factors as the interaction of adiposity and fitness was found nonsignificant ($p \geq .14$) across all measures. Classical assessments of body composition and aerobic fitness are highly related (% Body Fat relative to VO_2 max ml/kg/min: $r = -.75, p < .001$; BMI relative to VO_2 max ml/kg/min: $r = -.7, p < .001$), yet the utilization of DXA within the present investigation allowed for the dissociation of these factors (Total Fat Mass in kg relative to VO_2 max ml/kg of fat-free mass/min: $r = -.34, p < .001$) thereby reducing potential colinearity issues to enable the investigation of how these factors might interrelate relative to cognition. As the development of interventions aimed at improving cognitive control in typically developing preadolescent children continues; these findings suggest that fitness and adiposity can be considered as independent factors impacting cognitive health. The extent to which this relationship might change throughout maturation—particularly during puberty, still remains an open question.

In spite of the lack of an interaction between adiposity and aerobic fitness, the differential loading of adiposity and fitness on aspects of cognitive control is nevertheless intriguing. That is, inhibition, working memory, and cognitive flexibility represent distinct and distinguishable processes, but at the same time, they are considered functionally interrelated and share common neural structures (Miyake, Friedman, Emerson, Witzki, & Howerter, 2000). Thus, although these processes are predominately conceptual constructs, neuroimaging investigations have revealed a number of anatomical structures that are consistently activated in response to tasks requiring aspects of cognitive control. In particular, convergent evidence suggests that the neural network underlying cognitive control is primarily comprised of the prefrontal cortex, the anterior cingulate cortex (ACC), and the basal ganglia with additional contributions from the insular and parietal cortices as well as the superior frontal sulcus (SFS; Bunge & Crone, 2009; Ridderinkhof, Van Den Wildenberg, Segalowitz, & Carter, 2004; Rueda et al., 2005).

Consonant with this neuroanatomical perspective, the observation that aerobic fitness relates to both inhibition and cognitive flexibility is supported by a growing body of neuroimaging literature. Indeed, evidence from these investigations has begun to suggest that participation in physical activity and increased aerobic fitness is beneficial for neural regions involved with high-level cognitive processes. Specifically, findings in older-adult populations have indicated that aerobic exercise over a 6-month period served to ameliorate age-related declines in prefrontal and temporal brain areas (Colcombe et al., 2006). Cross-sectional investigations in both children and older adults have indicated that the relationship between aerobic fitness and indices of cognitive control are mediated by the dorsal striatum of the basal ganglia (Chaddock et al., 2010; Verstynen et al., 2012), as well as gray matter volume in the prefrontal cortex in older adult populations (Weinstein et al., 2012). Beyond structural differences, evidence suggests that greater physical activity participation and increased aerobic fitness in children is related to an enhanced ability to recruit neural tissues in the frontal and parietal regions (Chaddock, Erickson et al., 2012), modulation of activity in the ACC (Colcombe et al., 2004; Pontifex et al., 2011), and greater efficiency of neural networks underlying cognitive control (Voss et al., 2011).

Relative to body composition, the literature has largely focused on the relation of BMI to volumetric differences in the brain. Evidence from these investigations has indicated that obesity is related to decreased tissue volume in the frontal lobes, anterior cingulate gyrus, and hippocampus in older adults (Raji et al., 2010) and in the orbitofrontal cortex in adolescent children (Maayan et al., 2011). In contrast to these findings, Horstmann et al. (2011) observed a positive association between BMI and gray matter volume in the orbitofrontal cortex, nucleus accumbens, hippocampus, and left dorsal striatum in a young-adult population. Collectively, this body of research

provides early evidence to suggest a relationship between body composition and neural structures involved with the regulation of cognitive control. A limitation of these studies is their cross-sectional nature, necessitating further longitudinal research, which incorporates more precise measures of body composition to better understand the nature of the relationship between adiposity and these neural regions. Further elucidation is also warranted to examine the specific relations between adiposity and fitness relative to structural and functional changes within the brain.

Of much interest over the past decade are the cellular and molecular systems within the brain that may underlie these physical health related modulations in neural structures and functions. Indeed, one mechanism that has been posited for physical activity related enhancements in cognition is increases in cerebral blood flow, given evidence—in both mice and humans—that physical activity increases cerebral blood volume to the dentate gyrus of the hippocampus (Pereira et al., 2007). Similarly, alterations in neural vasculature resulting from the process of angiogenesis have been shown to occur in association with exercise in areas of the hippocampus, cortex, and cerebellum (Cotman, Berchtold, & Christie, 2007). These enhancements of neural support mechanisms may facilitate other cellular changes such as cellular proliferation, plasticity, and neurogenesis. Indeed, physical activity induced neurogenesis has been consistently observed in the nonhuman animal literature with voluntary physical activity resulting in alterations in the cytoarchitecture of the hippocampus—in particular the dentate gyrus—with increases in cellular proliferation, survival, as well as increases in dendritic length and complexity (Cotman et al., 2007; van Praag, Kempermann, & Gage, 1999). Among the molecular mechanisms for physical activity and fitness related differences in cognition, brain derived neurotrophic factor (BDNF) has been posited as a crucial mediator of exercise-induced enhancements in cognition (Gomez-Pinilla & Hillman, 2013). BDNF—a neurotrophic factor associated with the survival, growth, and differentiation of neurons—has been consistently found to increase in the hippocampus as a function of exercise participation. Most notably, inhibiting the binding of BDNF has been found to abolish exercise-induced enhancements in learning and memory in nonhuman animal models (Vaynman, Ying, & Gomez-Pinilla, 2004). Accordingly, accumulating evidence suggests that BDNF, and associated neurotrophic factors such as insulin-like growth factor (IGF1) and vascular endothelial growth factor (VEGF) may play a role in facilitating physical activity induced changes in cognition (Cotman et al., 2007; but see Gomez-Pinilla & Hillman, 2013 for review).

Interestingly, BDNF has also been found to play a major role in the regulation of energy metabolism with obese individuals exhibiting lower BDNF levels in the hippocampus (Rios et al., 2001). Similarly, Molteni, Barnard, Ying, Roberts, and Gómez-Pinilla (2002) found that a diet high in fats and refined sugar reduced BDNF in the hippocampus and impaired

synaptic plasticity and memory formation. Inversely, dysregulation of BDNF expression in mice is associated with increased caloric consumption and obesity (Rios et al., 2001). It would seem that both adiposity and fitness share common intracellular pathways by which changes in brain and cognition may be occurring. Given such similarity, the finding herein that adiposity and fitness did not interact is a bit surprising. However, given the complexity of these molecular systems it may be that adiposity and fitness exert their influences over branches of these molecular pathways (van Praag, 2009). An alternative, but not mutually exclusive perspective is that the present findings may be explained by other mechanisms beyond the shared molecular pathways between adiposity and fitness. Indeed, leptin, a hormone produced by adipose tissue, has been observed to elevate BDNF expression and independently modulates synaptic plasticity in the hippocampus (Gomez-Pinilla, 2008). Similarly, high-fat diets have been observed to alter plasma leptin and insulin levels, which served to dysregulate the dopamine receptor genes (McQuade, Benoit, Xu, Woods, & Seeley, 2004). Such genes have been found to be important for the regulation of behavior and are heavily involved in modulating activity within the ACC (Paus, 2001) and prefrontal cortex (Kröner, Krimer, Lewis, & Barrionuevo, 2007). Although refinement of such investigations utilizing animal models is still necessary to enhance the relevance for understanding the effects of physical health attributes on cognition in humans (Cotman et al., 2007); this body of literature provides some support for the overlapping but differentiated relationship between adiposity, fitness, and cognitive control.

Despite further research being necessary to better understand how other health behaviors and attributes (i.e., physical activity behaviors, dietary quality, sleep, etc.) collectively contribute to overall cognitive health, the present study provides new insights into the relationship between physical health and higher-order cognitive processes (i.e., cognitive control). Specifically, whereas adiposity and aerobic fitness are highly interrelated constructs, they may be differentially and independently related to the integrity of two core processes of cognitive control. Given growing public health concerns regarding both sedentary behavior and obesity, these data speak to the importance of health behaviors for cognitive health and effective functioning during childhood. Thus, these findings highlight a number of potential areas in which additional research is needed to provide a more comprehensive understanding of health and lifestyle factors that relate to cognitive function.

REFERENCES

- American College of Sports Medicine. (2006). *ACSM's guidelines for exercise testing and prescription* (7th ed.). New York: Lippincott Williams & Wilkins.

- Barkley, R. A. (1997). Behavioral inhibition, sustained attention, and executive functions: Constructing a unifying theory of ADHD. *Psychological Bulletin*, **121**, 65–94.
- Barlow, C. E., Kohl, H. W., Gibbons, L. W., & Blair, S. N. (1995). Physical fitness, mortality and obesity. *International Journal of Obesity and Related Metabolic Disorders*, **19**, S41–S44.
- Bar-Or, O. (1983). *Pediatric sports medicine for the practitioner: From physiologic principles to clinical applications*. New York: Springer-Verlag.
- Booth, F. W., & Lees, S. J. (2006). Physically active subjects should be the control group. *Medicine & Science in Sports & Exercise*, **38**, 405–406.
- Botvinick, M. M., Braver, T. S., Barch, D., Carter, C. S., & Cohen, J. D. (2001). Conflict monitoring and cognitive control. *Psychological Review*, **108**, 624–652.
- Bull, R., & Scerif, G. (2001). Executive functioning as a predictor of children's mathematics ability: Inhibition, switching, and working memory. *Developmental Neuropsychology*, **19**, 273–293.
- Bunge, S. A., & Crone, E. A. (2009). Neural correlates of the development of cognitive control. In J. Rumsey & M. Earnst (Eds.), *Neuroimaging in developmental clinical neuroscience* (pp. 22–37). New York: Cambridge University Press.
- Chaddock, L., Erickson, K. I., Prakash, R. S., VanPatter, M., Voss, M. W., Pontifex, M. B., et al. (2010). Basal ganglia volume is associated with aerobic fitness in preadolescent children. *Developmental Neuroscience*, **32**, 249–256. doi: 10.1159/000316648
- Chaddock, L., Erickson, K. I., Prakash, R. S., Voss, M. W., VanPatter, M., Pontifex, M. B., et al. (2012). A functional MRI investigation of the association between childhood aerobic fitness and neurocognitive control. *Biological Psychology*, **89**, 260–268. doi: 10.1016/j.biopsycho.2011.10.017
- Chaddock, L., Hillman, C. H., Pontifex, M. B., Johnson, C. R., Raine, L. B., & Kramer, A. F. (2012). Childhood aerobic fitness predicts cognitive performance one year later. *Journal of Sport Sciences*, **30**, 421–430. doi: 10.1080/02640414.2011.647706
- Church, T. S., Cheng, Y. J., Earnest, C. P., Barlow, C. E., Gibbons, L. W., Priest, E. L., et al. (2004). Exercise capacity and body composition as predictors of mortality among men with diabetes. *Diabetes Care*, **27**, 83–88.
- Colcombe, S. J., Erickson, K. I., Scalf, P. E., Kim, J. S., Prakash, R., McAuley, E. M., et al. (2006). Aerobic exercise training increases brain volume in aging humans. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, **61**, 1166–1170.
- Colcombe, S. J., Kramer, A. F., Erickson, K. I., Scalf, P., McAuley, E., Cohen, N. J., et al. (2004). Cardiovascular fitness, cortical plasticity, and aging. *Proceedings of the National Academy of Sciences of the United States of America*, **101**, 3316–3321. doi: 10.1073/pnas.0400266101
- Cotman, C. W., Berchtold, N. C., & Christie, L. (2007). Exercise builds brain health: Key roles of growth factor cascades and inflammation. *Trends in Neurosciences*, **30**, 464–472.
- Cserjési, R., Molnár, D., Luminet, O., & Lénárd, L. (2007). Is there any relationship between obesity and mental flexibility in children? *Appetite*, **49**, 675–678.
- Datar, A., & Sturm, R. (2006). Childhood overweight and elementary school outcomes. *International Journal of Obesity*, **30**, 1449–1460.
- Davidson, M. C., Amso, D., Anderson, L. C., & Diamond, A. (2006). Development of cognitive control and executive functions from 4 to 13 years: Evidence from manipulations of memory, inhibition, and task switching. *Neuropsychologia*, **44**, 2037–2078.
- Deák, G. O. (2004). The development of cognitive flexibility and language abilities. *Advances in Child Development and Behavior*, **31**, 271–327. doi: 10.1016/S0065-2407(03)31007-9

- Department of Health and Human Services [DHHS] and Department of Education [DOE]. (2000). *Promoting better health for young people through physical activity and sports. A report to the President from the Secretary of Health and Human Services and the Secretary of Education*. Silver Spring, MD: Centers for Disease Control.
- DeStefano, D., & LeFevre, J. (2004). The role of working memory in mental arithmetic. *European Journal of Cognitive Psychology*, **16**, 353–386.
- Donnelly, J. E., Greene, J. L., Gibson, C. A., Smith, B. K., Washburn, R. A., Sullivan, D. K., et al. (2009). Physical activity across the curriculum (PAAC): A randomized controlled trial to promote physical activity and diminish overweight and obesity in elementary school children. *Preventive Medicine*, **49**, 336–341.
- Eriksen, C. W., & Eriksen, B. A. (1974). Effects of noise letters upon the identification of a target letter in a non-search task. *Perception and Psychophysics*, **25**, 249–263. doi: 10.3758/BF03203267
- Espy, K. A. (1997). The shape school: Assessing executive function in preschool children. *Developmental Neuropsychology*, **13**, 495–499.
- Etnier, J. L., Salazar, W., Landers, D. M., & Petruzzello, S. J. (1997). The influence of physical fitness and exercise upon cognitive functioning: A meta-analysis. *Journal of Sport & Exercise Psychology*, **19**, 249–277.
- Frank, K. (2000). Impact of a confounding variable on the inference of a regression coefficient. *Sociological Methods and Research*, **29**, 147–194. doi: 10.1177/0049124100029002001
- Freedson, P. S., & Goodman, T. L. (1993). Measurement of oxygen consumption. In T. W. Rowland (Ed.), *Pediatric laboratory exercise testing: Clinical guidelines* (pp. 91–113). Champaign, IL: Human Kinetics.
- Gomez-Pinilla, F. (2008). Brain foods: The effects of nutrients on brain function. *Science and Society*, **9**, 568–578.
- Gomez-Pinilla, F., & Hillman, C. (2013). The influence of exercise on cognitive abilities. *Comprehensive Physiology*, **3**, 403–428. doi: 10.1002/cphy.c110063
- Goran, M., Fields, D. A., Hunter, G. R., Herd, S. L., & Weinsier, R. L. (2000). Total body fat does not influence maximal aerobic capacity. *International Journal of Obesity and Related Metabolic Disorders*, **24**, 841–848.
- Graziano, P. A., Calkins, S. D., & Keane, S. P. (2010). Toddler self-regulation skills predict risk for pediatric obesity. *International Journal of Obesity*, **34**, 633–641.
- Gunstad, J., Spitznagel, M. B., Paul, R. H., Cohen, R. A., Kohn, M., Luyster, F. S., et al. (2008). Body mass index and neuropsychological function in healthy children and adolescents. *Appetite*, **50**, 246–251.
- Hillman, C. H., Buck, S. M., Themanson, J. R., Pontifex, M. B., & Castelli, D. M. (2009). Aerobic fitness and cognitive development: Event-related brain potential and task performance indices of executive control in preadolescent children. *Developmental Psychology*, **45**, 114–129.
- Hillman, C. H., Erickson, K. I., & Kramer, A. F. (2008). Be smart, exercise your heart: Exercise effects on brain and cognition. *Nature Reviews Neuroscience*, **9**, 58–65.
- Hollar, D., Lombardo, M., Lopez-Mitnik, G., Hollar, T. L., Almon, M., Agatston, A. S., et al. (2010). Effective multi-level, multi-sector, school-based obesity prevention programming improves weight, blood pressure, and academic performance, especially among low-income, minority children. *Journal of Health Care for the Poor and Underserved*, **21**, 93–108.

- Hollar, D., Messiah, S. E., Lopez-Mitnik, G., Hollar, T. L., Almon, M., & Agatston, A. S. (2010). Effect of a two-year obesity prevention intervention on percentile changes in body mass index and academic performance in low-income elementary school children. *American Journal of Public Health, 100*, 646–653.
- Horstmann, A., Busse, F. P., Mathar, D., Müller, K., Lepsien, J., Schlögl, H., et al. (2011). Obesity-related differences between Women and Men in brain structure and goal-directed behavior. *Frontiers in Human Neuroscience, 5*, 1–9. doi: 10.3389/fnhum.2011.00058
- Kamijo, K., Khan, N. A., Pontifex, M. B., Scudder, M. R., Drollette, E. S., Raine, L. B., et al. (2012). The relation of adiposity to cognitive health and scholastic achievement in preadolescent children. *Obesity, 20*, 2406–2411. doi: 10.1038/oby.2012.112
- Kamijo, K., Pontifex, M. B., Khan, N. A., Raine, L. B., Scudder, M. R., Drollette, E. S., et al. (2012). The association of childhood obesity to neuroelectric indices of inhibition. *Psychophysiology, 49*, 1361–1371. doi: 10.1111/j.1469-8986.2012.01459.x
- Kamijo, K., Pontifex, M. B., Khan, N., Raine, L., Scudder, M., Drollette, E., & Hillman, C. H. (2014). The negative association of childhood obesity to the cognitive control of action monitoring. *Cerebral Cortex, 24*, 654–662. doi: 10.1093/cercor/bhs349
- Kamijo, K., Pontifex, M. B., O'Leary, K. C., Scudder, M. R., Wu, C.-T., Castelli, D. M., & Hillman, C. H. (2011). The effects of an afterschool physical activity program on working memory in preadolescent children. *Developmental Science, 14*, 1046–1058. doi: 10.1111/j.1467-7687.2011.01054.x
- Kane, M. J., & Engle, R. W. (2002). The role of prefrontal cortex in working-memory capacity, executive attention, and general fluid intelligence: An individual differences perspective. *Psychonomic Bulletin & Review, 9*, 637–671.
- Kaufman, A. S., & Kaufman, N. L. (1990). *Kaufman brief intelligence test manual*. Circle Pines, MN: American Guidance Service.
- Kröner, S., Krimer, L. S., Lewis, D. A., & Barrionuevo, G. (2007). Dopamine increases inhibition in the monkey dorsolateral prefrontal cortex through cell type-specific modulation of interneurons. *Cerebral Cortex, 17*, 1020–1032. doi: 10.1093/cercor/bh012
- Kuczmariski, R. J., Ogden, C. L., Guo, S. S., Grummer-Strawn, L. M., Flegal, K. M., Mei, Z., ... Johnson, C. L. (2002). 2000 CDC growth charts for the United States: Methods and development. *National Center for Health Statistics. Vital and Health Statistics, 11*(246), 1–1190.
- Lee, C. D., Blair, S. N., & Jackson, A. S. (1999). Cardiorespiratory fitness, body composition, and all-cause and cardiovascular disease mortality in men. *American Journal of Clinical Nutrition, 69*, 373–380.
- Lee, S., Kuk, J. L., Katzmarzyk, P. T., Blair, S. N., Church, T. S., & Ross, R. (2005). Cardiorespiratory fitness attenuates metabolic risk independent of abdominal subcutaneous and visceral fat in men. *Diabetes Care, 28*, 895–901.
- Li, Y., Dai, Q., Jackson, J. C., & Zhang, J. (2008). Overweight is associated with decreased cognitive functioning among school-age children and adolescents. *Obesity, 16*, 1809–1815.
- Lokken, K. L., Boeka, A. G., Austin, H. M., Gunstad, J., & Harmon, C. M. (2009). Evidence of executive dysfunction in extremely obese adolescents: A pilot study. *Surgery for Obesity and Related Diseases, 5*, 547–552.
- Maayan, L., Hoogendoorn, C., Sweat, V., & Convit, A. (2011). Disinhibited eating in obese adolescents is associated with orbitofrontal volume reductions and executive dysfunction. *Obesity, 19*, 1382–1387.

- MacDonald, A. W., Cohen, J. D., Stenger, V. A., & Carter, C. S. (2000). Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. *Science*, **288**, 1835–1838.
- McQuade, J.-A., Benoit, S. C., Xu, M., Woods, S. C., & Seeley, R. J. (2004). High-fat diet induced adiposity in mice with targeted disruption of the dopamine-3 receptor gene. *Behavioural Brain Research*, **151**, 313–319. doi: 10.1016/j.bbr.2003.09.034
- Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., & Howerter, A. (2000). The unity and diversity of executive functions and their contributions to complex “frontal lobe” tasks: A latent variable analysis. *Cognitive Psychology*, **41**, 49–100.
- Molteni, R., Barnard, R. J., Ying, Z., Roberts, C. K., & Gómez-Pinilla, F. (2002). A high-fat, refined sugar diet reduces hippocampal brain-derived neurotrophic factor, neuronal plasticity, and learning. *Neuroscience*, **112**, 803–814.
- Moore, R. D., Wu, C.-T., Pontifex, M. B., O’Leary, K. C., Scudder, M. R., Raine, L. B., et al. (2013). Aerobic fitness and intra-individual variability of neurocognition in preadolescent children. *Brain and Cognition*, **82**, 43–57. doi: 10.1016/j.bandc.2013.02.006
- Paus, T. (2001). Primate anterior cingulate cortex: Where motor control, drive and cognition interface. *Nature Reviews Neuroscience*, **2**, 417–424. doi: 10.1038/35077500
- Pereira, A. C., Huddleston, D. E., Brickman, A. M., Sosunov, A. A., Hen, R., McKhann, G. M., et al. (2007). An in vivo correlate of exercise-induced neurogenesis in the adult dentate gyrus. *Proceedings of the National Academy of Sciences*, **104**, 5638–5643. doi: 10.1073/pnas.0611721104
- Pontifex, M. B., Raine, L. B., Johnson, C. R., Chaddock, L., Voss, M. W., Cohen, N. J., et al. (2011). Cardiorespiratory fitness and the flexible modulation of cognitive control in preadolescent children. *Journal of Cognitive Neuroscience*, **23**, 1332–1345. doi: 10.1162/jocn.2010.21528
- Postle, B. R. (2006). Working memory as an emergent property of the mind and brain. *Neuroscience*, **139**, 23–38.
- Raji, C. A., Ho, A. J., Parikshak, N. N., Becker, J. T., Lopez, O. L., Kuller, L. H., et al. (2010). Brain structure and obesity. *Human Brain Mapping*, **31**, 353–364. doi: 10.1002/hbm.20870
- Ridderinkhof, K. R., Van Den Wildenberg, W. P., Segalowitz, S. J., & Carter, C. S. (2004). Neurocognitive mechanisms of cognitive control: The role of prefrontal cortex in action selection, response inhibition, performance monitoring, and reward-based learning. *Brain and Cognition*, **56**, 129–140.
- Rios, M., Fan, G., Fekete, C., Kelly, J., Bates, B., Kuehn, R., et al. (2001). Conditional deletion of brain-derived neurotrophic factor in the postnatal brain leads to obesity and hyperactivity. *Molecular Endocrinology*, **15**, 1748–1757. doi: 10.1210/me.15.10.1748
- Rogers, R. D., & Monsell, S. (1995). Cost of a predictable switch between simple cognitive tasks. *American Psychological Association*, **124**, 207–231.
- Rueda, M. R., Rothbart, M. K., McCandliss, B. D., Saccomanno, L., & Posner, M. I. (2005). Training, maturation, and genetic influences on the development of executive attention. *Proceedings of the National Academy of Sciences*, **102**, 14931–14936.
- Shvartz, E., & Reibold, R. C. (1990). Aerobic fitness norms for males and females aged 6 to 75 years: A review. *Aviation, Space, and Environmental Medicine*, **61**, 3–11.
- Spensley, F., & Taylor, J. (1999). The development of cognitive flexibility: Evidence from children’s drawings. *Human Development*, **42**, 300–324. doi: 10.1159/000022639

- St. Clair-Thompson, H. L., & Gathercole, S. E. (2006). Executive functions and achievements in school: Shifting, updating, inhibition, and working memory. *The Quarterly Journal of Experimental Psychology*, **59**, 745–759.
- Thomas, S., Reading, J., & Shephard, R. J. (1992). Revision of the physical activity readiness questionnaire (PAR-Q). *Canadian Journal of Sport Sciences*, **17**, 338–345.
- Utter, A. C., Robertson, R. J., Nieman, D. C., & Kang, J. (2002). Children's OMNI scale of perceived exertion: Walking/running evaluation. *Medicine & Science in Sports & Exercise*, **34**, 139–144.
- van Praag, H. (2009). Exercise and the brain: Something to chew on. *Trends in Neurosciences*, **32**, 283–290. doi: 10.1016/j.tins.2008.12.007
- van Praag, H., Kempermann, G., & Gage, F. H. (1999). Running increases cell proliferation and neurogenesis in the adult mouse dentate gyrus. *Nature Neuroscience*, **2**, 266–270. doi: 10.1038/6368
- Vaynman, S., & Gomez-Pinilla, F. (2006). Revenge of the “sit”: How lifestyle impacts neuronal and cognitive health through molecular systems that interface energy metabolism with neuronal plasticity. *Journal of Neuroscience Research*, **84**, 699–715. doi: 10.1002/jnr.20979
- Vaynman, S., Ying, Z., & Gomez-Pinilla, F. (2004). Hippocampal BDNF mediates the efficacy of exercise on synaptic plasticity and cognition. *European Journal of Neuroscience*, **20**, 2580–2590. doi: 10.1111/j.1460-9568.2004.03720.x
- Verstynen, T. D., Lynch, B., Miller, D. L., Voss, M. W., Prakash, R. S., Chaddock, L., et al. (2012). Caudate nucleus volume mediates the link between cardiorespiratory fitness and cognitive flexibility in older adults. *Journal of Aging Research*, **2012**, 1–11. doi: 10.1155/2012/939285
- Voss, M., Chaddock, L., Kim, J., VanPatter, M., Pontifex, M., Raine, L., et al. (2011). AT Aerobic fitness is associated with greater efficiency of the network underlying cognitive control in preadolescent children. *Neuroscience*, **199**, 166–176. doi: 10.1016/j.neuroscience.2011.10.009
- Weinstein, A. M., Voss, M. W., Prakash, R. S., Chaddock, L., Szabo, A., White, S. M., et al. (2012). The association between aerobic fitness and executive function is mediated by prefrontal cortex volume. *Brain, Behavior, and Immunity*, **26**, 811–819. doi: 10.1016/j.bbi.2011.11.008
- Yokum, S., Ng, J., & Stice, E. (2012). Relation of regional gray and white matter volumes to current BMI and future increases in BMI: A prospective MRI study. *International Journal of Obesity*, **36**, 656–664.