THE NEGATIVE INFLUENCE OF ADIPOSITY EXTENDS TO INTRAINDIVIDUAL VARIABILITY IN COGNITIVE CONTROL AMONG PREADOLESCENT CHILDREN

BY

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THESIS

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Abstract

Objective: To investigate the relationship between adiposity and cognition using mean accuracy, mean reaction time, and intraindividual variability (IIV) among preadolescents.

Methods: Children 7-9 years old (N=233, 133 females) underwent dual-energy x-ray absorptiometry and a VO_2peak test to assess whole-body adiposity and aerobic fitness relative to fat-free mass (VO_2FF), respectively. Attentional inhibition was assessed using a modified flanker task. IIV was assessed as standard deviation (SDRT) and coefficient of variation (CVRT) of response time. Hierarchical linear regression analyses were performed to examine the relationships between adiposity and cognitive measures following adjustment of significant demographic factors, intelligence quotient, and VO_2FF.

Results: Whole-body adiposity was negatively related to congruent trial mean accuracy and reaction time and to CVRT in both the congruent and incongruent trials. Differences in cognitive function across weight status were selectively evident for measures of IIV such that children with overweight/obesity ($\geq 85^{th}$ BMI-for-age percentile) exhibited higher CVRT for both the congruent and incongruent trials.

Conclusion: This work provides additional evidence linking childhood obesity to poorer cognitive function and includes novel data extending the negative influence of adiposity to measures of intraindividual response variability in cognitive control, even after accounting for intellectual abilities, aerobic fitness and demographic factors.

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CHAPTER 1 - REVIEW OF THE LITERATURE

1.1 Overview

Worldwide obesity has nearly tripled since 1975 with more than 1.9 billion adults living with overweight and 650 million are living with obesity[1]. As of 2016, over 340 million children and adolescents over age 5 were living with overweight or obesity and over 41 million children under the age of 5 were living with overweight or obesity[1]. In the United States in 2015-2016, the prevalence of obesity was 39.8% in adults and 18.5% in youth[2]. Obesity is known to contribute to numerous health and psychosocial problems, including but not limited to cardiovascular disease[3], metabolic syndrome[3], diabetes mellitus type 2[3], Alzheimer's disease[4], dementia[4], poorer educational attainment[5], higher rates of poverty[5], and lower household income[5]. Additionally, excess fat mass has been correlated with impaired cognitive performance[13,19–22]. While overweight and obesity are negatively related to cognitive control, aerobic fitness is positively related to cognitive control[11–16], yet the two are seldom studied together.

1.2 Childhood Obesity

Childhood obesity is a growing worldwide epidemic that places extreme burden on the healthcare system[17]. The CDC defines obesity as at or above the 95th percentile BMI-for-age and overweight as between the 85th and 95th percentile BMI-for-age[18]. Overweight and obesity affects as many as 34% of children in the USA[19]. Causes of childhood obesity are still being extensively studied. There are the generally recognized factors that lead to obesity such as increased fast food consumption, increased sugary beverage consumption, associations with junk food being pleasurable, increased portion sizes, and sedentary lifestyles; however, while it is widely accepted that obesity results from energy intake and expenditure imbalances, there is increasing evidence that both genetics and epigenetics play a role as well[20–22]. The ecological model explains that childhood risk factors for obesity include dietary intake, physical activity, and sedentary behavior; which are in turn moderated by age, gender, family characteristics, parenting style, parents' lifestyle, school policies, and demographics[23]. Soubry et al found that children born to obese parents, as compared to children born to non-obese parents, have altered methylation outcomes at multiple imprint regulatory regions suggesting that parental lifestyle preconception can lead to reprogramming during gametogenesis and early development leading to instability carried onto the next generation[22]. Guenard et al compared siblings born to mothers pre- and post- weight loss surgery and found differences between siblings in their methylation profiles for genes involved in the regulation of glucose and immune function which lead to alterations in gene expression and insulin sensitivity[24,25]. Some studies have even found that BMI is up to 40% heritable, but there seems to be consensus that the genetic susceptibility needs to be coupled with environmental and/or behavioral factors to truly affect weight[20,26].

Medical expenses for obesity have escalated to 40% of the healthcare budget[19]. This includes expenses for prescription drugs, outpatient appointments, and emergency department visits for children (6-19 years old) with elevated BMIs[19]. The increase in medical expenses can be explained by the association between obesity and increased risk of dyslipidemia, hypertension, sleep-disordered breathing, nonalcoholic fatty liver disease, and polycystic ovarian syndrome[27]. Childhood obesity is thought to serve an important factor in the genesis of type 2 diabetes mellitus and coronary heart disease[20,28]. Excess adiposity, even as early as childhood, is indicated by the presence of inflammatory markers, markers of oxidative stress, and endocrine abnormalities such as insulin resistance[29]. These instabilities are thought to be the drivers for all of the factors associated with metabolic syndrome, and children who develop metabolic syndrome have a 3 fold greater likelihood of type 2 diabetes mellitus and cardiovascular issues[29]. In addition, childhood obesity is linked to asthma, hepatic steatosis, gallstones, skin conditions, menstrual abnormalities, impaired balance, and orthopedic problems[20]. Children with obesity also are reported to have poor academic performance and lower quality of life[20], There is also a Catch 22 where the social consequences of obesity such as low self-esteem, low self-confidence, and negative body image cause children to protect themselves by retreating to safe places and resorting to comfort foods[30]. While it is clear that the medical and psychosocial consequences are vastly studied, there is still a gap in the study of cognitive implications of obesity.

1.3 Cognitive Control

Also called executive function, cognitive control encompasses the mental processes that underlie goal-directed behavior and are orchestrated by activity within the prefrontal cortex[31]. The foundational executive functions can be broken down into three categories: inhibition, working memory, and cognitive flexibility[31]. Inhibition refers to the mind's ability to suppress interference and selectively attend to relevant stimuli; working memory is responsible for temporarily holding information available for processing; and cognitive flexibility involves the ability to redirect attention between one task or rule set and another[31]. All three are important for and take part in processing, decision making, and behavioral and emotional regulation[31].

1.3.1 Inhibitory control

Inhibitory control is one of the core cognitive control processes and it specifically refers to the ability to ignore distracters and selectively focus on the relevant factors in the stimulus environment[31]. In children, inhibitory control is associated with early literacy and numeracy advantage throughout the early school years and is implicated in children's overall learning[32,33] as well as other behavioral, social, and emotional competencies[34,35]. Additionally, deficiency in inhibitory control is often observed among individuals with ADHD[36], schizophrenia[37], autism[38], and obsessive-compulsive disorders[39]. Inhibitory control is important in the real world because it allows people to selectively attend, or rather, focus on to the task at hand while suppressing other distracting stimuli around them[40]. The ability to ignore particular stimuli and attend to others is considered attentional inhibition (or inhibition of attention)[40]. Attentional inhibition is the area of inhibitory control that is often studied in research using tasks such as the Flanker task and the Stroop task[40]. Another component of inhibitory control is the ability to suppress extraneous thoughts or memories which can be referred to as cognitive inhibition[40]. The third component of inhibitory control is behavioral inhibition, or self-control; the ability to stay on task despite distractions and temptations to give up[40]. The cognitive inhibition and behavioral inhibition aspects are both larger parts of total behavioral regulation which is needed in day to day activities keeping impulsive behaviors internalized. They can be grouped together as response inhibition (or inhibition of action) which is studied in research using tasks such as the Go/NoGo and Stop-Signal tasks[40]. Attentional inhibition and response inhibition are strongly correlated with each other[40].

1.3.2 Flanker Task

The Eriksen Flanker task measures attentional inhibition but requires a small amount of working memory as well[31,41]. Modified versions of the Flanker task are used in numerous physical activity and adiposity studies[10,42,43], developmental studies[44–46], and intraindividual variability studies[12,13,47–49], all studying effects on cognition. Briefly, the task requires an individual to focus on a centrally located (target) stimulus amid an array of four task-irrelevant distracter stimuli. The task has two conditions comprised of congruent and incongruent trials. During the congruent trials all stimuli face the same direction, whereas in the incongruent trials, the target stimulus faces the opposite direction of the flanking stimuli. The incongruent trials require upregulation of inhibitory control when compared to the congruent trials, therefore it is expected that reaction time will be slower and accuracy will be decreased during the incongruent trials[50].

1.3.3 Central Tendency in Cognitive Control

Performance during cognitive tasks is often assessed based on central tendency measures i.e., mean accuracy and reaction time of correct responses[13]. Thus, central tendency focuses on the mean differences in performance and reaction time[51], providing limited information on fluctuations in within individual performance or dispersion (more below). Additionally, the pressure to respond quickly can contaminate an accuracy experiement[52]. Although study subjects are explicitly instructed to be accurate, there tends to be a speed-accuracy trade-off in that participants want to respond quickly more than they want to respond accurately[52]. MacDonald and Stuart point out that while measures of central tendency capture meaningful performance differences when task performance is relatively consistent, using central tendency can lead to biased estimates of performance[53].

1.3.4 Dispersion in Cognitive Control

Measures of dispersion are also acquired during cognitive tasks and specifically refers to intraindividual variability (IIV), or the within-person fluctuation in behavioral performance[13]. Essentially, IIV provides insight into cognitive control consistency during task performance. IIV can be measured as either standard deviation of reaction time (SDRT) or coefficient of variation of reaction time (CVRT). CVRT is the SDRT relative to the mean reaction time. Lower values for measures of IIV are desirable as increased IIV has been shown to characterize aging[54], dementia[55,56], head injury, ADHD[57], major depression[58], borderline personality disorder[58], and schizophrenia[58].

While much of the current cognitive research focuses on central tendency, or the mean differences between groups in measures such as accuracy and reaction time, IIV may provide a more sensitive measure of cognitive control[59]. IIV in performance uses small differences that provide useful predictive information whereas central tendency calculates mean performance from a single measurement which can lead to flawed estimates of average group differences[53,60]. Specifically, IIV can provide predictive information above mean performance and can make population differences more apparent[56,59,61]. While studies show that reaction time and SDRT are correlated, they actually reflect independent sources of variance[59]. Jensen, et al, found that both RT and SDRT are important to study as they reflect different processes that are independently correlated with elementary cognitive processes[59]. As mentioned above, RT would reflect the speed of information processing where as SDRT would reflect the consistency in processing speed[59].

It is important to note that IIV follows a U-shaped curve over the course of normal aging.: as a young child, IIV will be higher and will decrease through adolescence and stabilize in adulthood, then will increase again in older adulthood[62,63]. This is comparable to the inverted U-shape that cognitive function follows with young children exhibiting lower cognitive function, improvement through adulthood, then decline in older adulthood[64]. However, IIV has also been linked to biomarkers of age such as grip strength[65] and visual acuity[65], and greater IIV can predict risk of mortality from all causes regardless of age[66], suggesting that IIV is a behavioral indicator of CNS integrity and frontal-cortex-mediated processes (i.e. cognitive control and attentional lapses)[67].

1.4 Overweight and Obesity and Cognitive Control

Recent research has revealed that increased adiposity, independent of medical issues associated with obesity, is associated with poor cognitive control[51]. Studies show that, age-independent, adipose tissue chronically activate the inflammatory response by producing proinflammatory cytokines[68]. Inflammation can have profound effects in multiple brain areas[69]and is also associated with reduced spatial learning and memory skills[70] as well as interference in synaptic communication in the hippocampus[71]. Overall, it is has been observed that the hormones that regulate metabolism also play a significant role in cognitive processing components that are key to cognitive control[68].

One study examined 408 healthy adults across the lifespan (20 to 82 years old) to determine whether BMI and cognitive performance varied with age[72]. The researchers observed that, regardless of age, overweight and obese adults exhibited poorer cognitive control when compared to healthy weight adults, and that the relationship does not vary with age[72]. Similarly, the Baltimore Longitudinal Study on Aging examined 1703 adults to determine whether central obesity would be more closely associated with cognitive function and determined that multiple indices of obesity were related to poorer performance in multiple cognitive domains, regardless of age of the subject[73].

An increasing body of literature recognizes that obesity is also related to poorer cognitive function in children and adolescents. A study with 525 adolescents in grades 6 and 7 used a modified Flanker test to assess inhibitory control and found that a higher BMI was negatively associated with accuracy and interferences[74]. Further, waist circumference and was negatively associated with accuracy and positively associated with reaction time in the same task[74]. Among preadolescents, Kamijo et al found that obese children exhibited longer reaction time than healthy weight children during the incompatible condition of a modified Flanker task, suggesting that childhood obesity is related to a poorer ability to modulate cognitive control when task demands increase[10]. The negative influence of obesity has also been extended to academic achievement. For example, in a large study among 9-11-year-olds (N=893), Torrijos-Ni and colleagues observed that obese boys had lower academic achievement scores than overweight or normal weight boys[75]. Additionally, higher BMI and fat mass were associated with lower academic achievement[76]. In a longitudinal study, Datar et al found that change in overweight status between kindergarten and grade 3 was a significant risk factor for poorer test scores and adverse school outcomes among girls by the end of third grade[77]. Additionally, girls who began kindergarten overweight had more behavioral problems by the completion of third grade[77].

1.5 Aerobic Fitness and Cognitive Control

An emerging body of literature supports the benefits of physical activity on cognitive function across a variety of cognitive domains. These data have emerged from studies in both animal and human models. Recent animal studies have focused on elucidating the molecular and physiological underpinnings of the relationship between exercise provision and changes brain function. Findings from animal studies have observed that exercise activates molecular and cellular cascades that support brain plasticity[78]. In addition, exercise induces expression of genes associated with plasticity and promotes brain vascularization, neurogenesis, and functional changes in neuronal structure and neuronal resistance to injury[78]. Voluntary exercise in the form of wheel running, and not forced exercise in the form of yoked-swimming, enhanced neurogenesis in adult mice, resulting in a two-fold increase in the number of surviving newborn cells in the hippocampus[79].

Among humans, studies in older adults have revealed that exercise provision has the potential to reduce age-related cognitive decline. In a randomized control trial among 2049 adults 18 or older, participation in an aerobic exercise intervention for longer than one month was associated with modest improvements in attention and processing speed, cognitive control, and memory[80]. Another study among 66 adults (18 to 48 years old) found that increasing physical activity by 15% or more was related to improved scores on memory and recall[81]. Additionally, in otherwise healthy, but sedentary older adults, there are robust but selective benefits of fitness training for cognitive control processes[82]. The benefits of greater fitness have also been demonstrated for brain structure, as evidenced by magnetic resonance imaging (MRI) studies. For example, in a study with 55 older adults (mean age 67 years), there were substantially reduced declines in frontal, parietal, and temporal tissue densities in adults with greater aerobic fitness[83]. In fact, another study of 59 older adults (60 to 79 years old) found that there were significant increases in both gray and white matter volume in older adults that participated in an aerobic fitness training internvention[84]. In another year-long exercise intervention with 70 older adults (55 to 80 years old), aerobic fitness training from a walking program was associated with a greater change in white matter integrity in both the frontal and temporal lobes and greater improvements in short-term memory[85]. An eight-week intervention of older adults (mean age 62 years) showed significant improvement in accuracy and recall scores after practicing Hatha yoga[86]. All of these studies point to consistent positive relationships between cognitive performance and exercise and suggest that exercise interventions can be extremely beneficial in the older adult population.

There is a growing effort to better understand the effects of exercise on improvement in cognition and academic achievement in children specifically due to the decline in overall physical activity in children as well as reductions in physical education and school recess. Currently, only

27% of high school students in the United States meet the pediatric physical activity guidelines of 60 minutes of daily moderate-to-vigorous activity (MVPA)[87]. Belcher et al observed that in a study among 3106 children (6 to 19 years old), children ages 6-11 spent the most time in MVPA (88 minutes/day) when compared to children ages 12-15 (33 minutes/day) and children ages 16-19 (26 minutes/day)[88]. These results indicate that only 42% of the children in this study met the physical activity guidelines, and of those, the non-Hispanic black children ages 6-11 were the most likely to meet the guidelines[88]. The decline in physical activity as children get older is supported by a meta-analysis by Hollis et al that found that during physical education classes, middle school students only spent 48.6% in MVPA and high school students only spent 34.7% in MVPA, both of which fall short of the US Center for Disease Control and Prevention recommendations of 50%[89]. According to the CDC School Health Policies and Programs Study, only 4% of elementary schools provided daily physical education (150 minutes per week) and 14% provided physical education 3 days per week[90]. Additionally, only 65% of elementary schools provided children with regularly scheduled recess, and 55% provided less than 30 minutes of recess time[90]. With these declines in physical activity, physical education, and recess in the United States, the cognitive implications need to be better understood.

Numerous physical activity, cognition, and academic achievement studies have been conducted. In a study comparing 38 higher-fit and lower-fit children (mean age 9.4 years), data suggests that fitness is associated with better cognitive performance on a modified Flanker task designed to test cognitive control[14]. Another study with 36 children (9 to 10 years old) found that lower-fit children had disproportionate accuracy performance cost as task difficulty increased than the higher-fit children[91]. Interestingly, another study involving 18 lower-fit and 14 higher-fit children (9 to 10 years old) found that higher-fit children demonstrated increased accuracy in a

Flanker task as well as a better strategy to switch between task conditions during both baseline and follow-up appointments[92]. They also gained a speed benefit during follow-up testing[92]. The aforementioned studies suggest that aerobic fitness relates to cognitive control at the time of fitness testing, but may also play a role in cognitive performance in the future[92]. One study that looked at 94 overweight but otherwise healthy children (7 to 11 years old) showed that the high-dose exercise group displayed improved post-test scores in cognitive control and planning scores[93]. Another study examined 171 overweight and inactive children (7 to 11 years old) and found that there was a dose response of exercise on cognitive control as well as mathematics achievement, and there was reduced bilateral posterior parietal cortex activity[94]. In another study of twenty children (8 to 10 years old), researchers found that an acute bout of exercise, whether intermittent or continuous, improved cognitive control in children with effects maintained for approximately thirty minutes following cessation[95]. Another study looked at 893 school-aged children (9 to 11 years old) and found that overall academic achievement scores were positively related to fitness levels[75]. Krafft et al studied 43 unfit, overweight children (8 to 11 years old) who participated in one of two 8 month after-school interventions: either a 40 minute aerobic exercise intervention or an attention control intervention that involved instructor-led sedentary activities[96]. Results showed that when compared to the control group, the exercise group fMRI results displayed increased activation in several regions during the Flanker performance, but there were no significant group differences in accuracy or reaction time results[96]. Hillman et al also conducted an RCT with 221 children (7 to 9 years old) that were randomly assigned to either a 9-month after-school fitness program or a wait-list control[97]. The results demonstrated that while fitness improved in the children participating in the intervention, so did inhibition and cognitive flexibility[97]. They also found that improvements in brain function during both the inhibition task and the flexibility task correlated with intervention attendance[97].

1.6 Differential Associations of Fitness and Adiposity on Cognitive Function

Most studies, as examined above, focus on the impact of just adiposity or just aerobic fitness on cognition. However, the overlapping or independent influence of aerobic fitness and adiposity on childhood cognitive control has not been directly examined. Indeed, the literature on these topics has been disparate such that one body of work has examined the influence of fitness on cognitive control while another has focused on the influence of adiposity[51,98]. Considering the conceptual and physiological overlaps between fat mass and aerobic fitness, there needs to be a shift to focus on the possible inter-relationship between obesity and fitness and cognition. One study examined 70 children (9 to 10 years old) during a six-month physical activity program with cognitively demanding skills or a curricular physical education only[99]. The study found that higher-fit children displayed better inhibitions and that overweight children had a more pronounced improvement from the intervention independent of aerobic fitness gains[99]. Another study in Finland included 8061 children with reported motor function at 8 years old and obesity, fitness, and self-reported physical activity level at age 16[100]. They found that physical activity was associated with a higher GPA while obesity was associated with a lower GPA[100]. Also, compromised motor function during childhood had a negative effect on adolescent academic achievement through both physical inactivity and obesity but not fitness[100]. These results imply that physical activity and obesity, together, may mediate the association between motor function and academic achievement[100]. Pontifex et al examined the differential associations between obesity, aerobic fitness, and cognition in a sample of 204 children (9 to 10 years old)[101]. They observed that fitness was independently associated with inhibition and cognitive flexibility, while adiposity was independently associated with cognitive flexibility[101]. However, when observed together, there was no significant relationship. This suggests that the two may be differentially associated with specific components of cognitive control [101].

Clearly additional work is needed to elucidate the impact of both fitness and adiposity on children's cognitive control. In addition to the gap in literature examining fitness and adiposity together, more work is needed on specific measures of cognitive function vulnerable to the impact of childhood obesity. With a disproportionate focus on central tendency, we believe that IIV may be a more sensitive measure of cognition in children focusing on the within-person fluctuations rather than mean differences. It can provide insight into the underlying consistency of cognitive control. By examining adiposity and fitness together, as well as central tendency and IIV measures, we will provide novel insight into the nature of these relationships and their sensitivity in childhood obesity studies.

CHAPTER 2 – THE NEGATIVE INFLUENCE OF ADIPOSITY EXTENDS TO INTRAINDIVIDUAL VARIABILITY IN COGNITIVE CONTROL AMONG PREADOLESCENT CHILDREN [1]

2.1 Abstract

Objective: To investigate the relationship between adiposity and cognition using mean accuracy, mean reaction time, and intraindividual variability (IIV) among preadolescents.

Methods: Children 7-9 years old (N=233, 133 females) underwent dual-energy x-ray absorptiometry and a VO_2peak test to assess whole-body adiposity and aerobic fitness relative to fat-free mass (VO_2FF), respectively. Attentional inhibition was assessed using a modified flanker task. IIV was assessed as standard deviation (SDRT) and coefficient of variation (CVRT) of response time. Hierarchical linear regression analyses were performed to examine the relationships between adiposity and cognitive measures following adjustment of significant demographic factors, intelligence quotient, and VO_2FF.

Results: Whole-body adiposity was negatively related to congruent trial mean accuracy and reaction time and to CVRT in both the congruent and incongruent trials. Differences in cognitive function across weight status were selectively evident for measures of IIV such that children with overweight/obesity ($\geq 85^{th}$ BMI-for-age percentile) exhibited higher CVRT for both the congruent and incongruent trials.

Conclusion: This work provides additional evidence linking childhood obesity to poorer cognitive function and includes novel data extending the negative influence of adiposity to measures of

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intraindividual response variability in cognitive control, even after accounting for intellectual abilities, aerobic fitness and demographic factors.

2.2 Introduction

Currently, one in three children in the United States has overweight/obesity ($\geq 85^{th}$ BMI-for-age percentile)[102], which is concerning given that obesity contributes to numerous chronic diseases including cardiovascular disease, metabolic syndrome, and diabetes mellitus type 2[3]. In addition to its cardiovascular and metabolic implications, obesity in midlife is also a known risk factor for adverse cognitive health outcomes including greater risk for Alzheimer's disease and dementia[4]. Further, psychosocial consequences of obesity include poorer educational attainment, higher rates of poverty, and lower household income[5]. Given the detrimental relationship of obesity on cardiovascular disease and cognitive heath in adulthood, the question of whether these relationships are evident in childhood has received increased scrutiny.

A converging body of literature indicates that greater aerobic fitness, as early as preadolescence, promotes superior cognitive performance, and alterations in brain structure and function[98]. Cognitive control encompasses a complex set of goal-directed processes including attention, memory, learning, and perception[103], and has been shown to be positively related to greater aerobic fitness. Improved cognitive control during development is predictive of later academic achievement and has been linked to greater educational attainment, higher income and socioeconomic status, as well as better access to health care[104]. In contrast to fitness effects on the brain, mechanisms underlying how obesity or excess fat mass influence cognitive control are not clear, although indirect mechanisms involving adipocyte-induced neuroinflammation have received considerable attention[105]. Excess adiposity can lead to increased levels of circulating free fatty acids, pro-inflammatory cytokines, and immune cells, which in turn may contribute to neuroinflammation[105,106]. For example, proinflammatory cytokines such as IL-6 and TNFα are known to exert neurodegenerative effects in several brain diseases[105,107]. Additionally, inflammation and oxidative stress often co-exist and oxidative stress is associated with astrocyte activation, brain pro-inflammatory cytokine production, and cognitive impairment[105,108]. Although additional research is needed to illustrate the mechanisms by which adiposity affects cognitive function, correlational and longitudinal studies often support a negative relationship between obesity and cognitive control[51]. Given the inverse relationship between obese weight status and poorer aerobic fitness, these physiological factors likely impart counteractive effects on cognitive control, yet the two are seldom examined together. Therefore, relatively little is known about the influence of adiposity on children's cognitive function while accounting for fitness.

In addition to limited research examining the cognitive implications of childhood obesity while accounting for fitness, additional work is required to characterize the specific measures of cognitive function susceptible to the influence of childhood obesity. Previous cognitive and neuropsychological research has disproportionately focused on measures of central tendency, such as mean differences in performance[51], across individuals while neglecting measures of within individual variability, therefore limiting our understanding of the true extent to which obesity may influence children's cognitive function. Intraindividual variability (IIV) provides metrics of within-person fluctuations in behavioral performance and offers insight into the degree of consistency in cognitive control during task performance[13]. Specifically, intraindividual standard deviation of reaction time (SDRT) and intraindividual coefficient of variation of reaction time (CVRT) can serve as useful indices of patterns of behavioral responses that underlie the consistency of cognitive control performance and have been previously shown to have relevance for a number of cognitive abilities in everyday life as well as to the study of neurological disease[109]. However, the extent to which childhood obesity may impact IIV during cognitive control tasks has not been directly examined. Accordingly, the objective of the present study was to investigate the relationships between adiposity and cognitive performance using measures of central tendency and intraindividual variability, while accounting for demographical factors and aerobic fitness.

2.2.1 Hypothesis

We hypothesized that greater adiposity would be related to poorer mean performance as well as higher IIV among preadolescent children. We also anticipated that children with overweight and obesity would have significantly higher IIV relative their healthy weight counterparts.

2.3 Methodology

2.3.1 Participants

Participants were 7-9-year-old preadolescent children recruited as part of the FITKids2 randomized controlled trial, a physical activity after-school intervention program assessing the effect of daily exercise on cognitive function between 2013 and 2017 (NCT01619826). Children who completed all tasks (N=233) were included at their baseline measurement, prior to randomization and intervention. Exclusion criteria included neurological disorders, physical disabilities, and psychoactive medication use, as reported by parents in an eligibility questionnaire. All participants were required to have normal or corrected-to-normal vision. Participants provided written assent and their legal guardians provided written consent in accordance with the ethical standards and regulations of the Institutional Review Board (IRB) at the University of Illinois at Urbana-Champaign (IRB #12321).

2.3.2 Procedure

Testing occurred over two laboratory visits. During the first visit, participants completed informed assent/consent, the Woodcock Johnson Test of Cognitive Abilities to estimate intelligence quotient (IQ), measurement of height and weight, and a maximal oxygen consumption test (VO_2peak)[110] to assess aerobic fitness. Concurrently, parents completed surveys assessing demographics, health history, and pubertal status according to the modified Tanner Staging Scales[111,112]. Socioeconomic status (SES) was determined from eligibility for school meal-assistance programs, maternal and paternal education levels, and the number of parents with full-time employment. During the second visit, participants completed a modified flanker task[41] designed to assess attentional inhibition, and a Dual-Energy X-ray Absorptiometry (DXA) assessment of whole body and visceral adiposity.

2.3.3 Intelligence Quotient Assessment

The Woodcock Johnson Test of Cognitive Abilities was used to estimate IQ. Tests include audio recordings, subject response booklet, and subject response pages. The test is individually administered by a trained examiner based on the guidelines provided in the Examiner's Manual[113]. Basal and ceiling criteria are listed in the Test Book for each subtest and raw scores are calculated for each test. Test and cluster scores are then calculated using the Woodcock Johnson III Normative Update Compuscore and Profiles program (Compuscore; Schrank & Woodcock, 2007).

2.3.4 Pubertal Stage Assessment

The modified Tanner Staging Scales were presented to the parents as a document with five separate line drawings depicting various stages of external genitalia development (males), breast development (females), and pubic hair development (males and females). Parents were asked to identify the line drawing that depicted their child's developmental status and the average of scores was used to determine the child's pubertal stage. Previous research has validated the Tanner Scale in different samples of children and has shown good agreement with clinician examination with kappa values ranging from 0.68 to 0.76[112,114].

2.3.5 Anthropometric and Adiposity Assessment

Participants height and weight were measured, without shoes, using a stadiometer (model 240; Seca, Hamburg, Germany) and a Tanita WB-300 Plus digital scale (Tanita, Tokyo, Japan), respectively. Each measurement was taken three times and the average was used for analyses. BMI-for-age-percentile cut-offs from the CDC were used to determine weight status[115]. Fat mass and muscle mass were measured using DXA with a Hologic Discovery A bone densitometer (software version 12.7.3; Hologic, Bedford, MA). Whole-body adiposity (%Fat) was expressed using the standard software measure[116].

2.3.6 Cardiorespiratory Fitness Assessment

Maximal aerobic capacity (VO_2peak) was assessed using a modified Balke treadmill protocol[110]. This modification involved maintaining a constant speed of the treadmill while increasing the workload (i.e., grade) of the treadmill. The modified Balke protocol follows the ACSM Guidelines for Exercise Testing and Prescription[117,118] in children and is regarded as valid and reliable for estimating cardiorespiratory fitness in children[119]. Children were then fitted with a heart rate monitor (Polar WearLink + 31, Polar Electro, Finland) for the duration of the assessment. Children started with a warm-up period, and then jogged at a constant speed with increasing grade increments of 2.5% every 2 minutes until perceived exhaustion. Oxygen consumption was measured using a computerized indirect calorimetry system (True Max 2400; ParvoMedics, Sandy, Utah) with averages for oxygen uptake and respiratory exchange ratio assessed every 20 seconds. Concurrently, ratings of perceived exertion (RPE) were measured every 2 minutes using the children's OMNI rating of perceived exertion scale. VO_2peak was defined as the highest oxygen consumption corresponding to a minimum of 2 of the following 4 criteria: (1) a peak heart rate ≥185 beats per minute, (2) a respiratory exchange ratio > 1.0, (3) a RPE score of ≥8, and/or (4) a plateau in oxygen consumption corresponding to an increase of <2 mL/kg/min despite an increase in workload[110]. Aerobic fitness percentiles were determined by using normative values for VO2peak[120]. Absolute VO_2peak (L/min) was adjusted for fat-free mass (from DXA) to calculate fat-free VO_2peak (VO_2FF). Prior to VO_2peak assessment, all participants completed the Physical Activity Readiness Questionnaire (PAR-Q) to screen for contraindications to physical activity[121]. Further, each assessment was conducted by a minimum of at least 3 trained staff members with certification in cardiopulmonary resuscitation (CPR) and automated external defibrillator (AED) administration.

2.3.7 Attentional Inhibition Assessment

A modified flanker task[41] presented a target stimulus (cartoon fish) amid an array of four flanking stimuli. Participants were asked to respond to the centrally presented target with the flanking stimuli irrelevant to the task. This modified version of the flanker task consisted of both congruent trials, where the flanking fish faced the same direction as the target fish (> > > > >), and incongruent trials, where the flanking fish faced the opposite direction from the target fish (> > < > >)[122]. Congruent and incongruent trials were equiprobable and random. Participants responded to the direction of the target fish, left or right, with their consonant thumb. Participants completed 54 practice trials followed by two blocks of 84 trials. The viewing distance was 1 meter, the stimulus duration was 250 milliseconds, and the interstimulus interval was jittered at 1600, 1800, or 2000 milliseconds. For behavior data, primary variables of interest included mean response time (time in ms from stimulus presentation until response execution), response accuracy (percentage of correct responses), standard deviation (SDRT), and coefficient of variation (SD/Mean RT) of reaction time (CVRT) for all correct trials types (congruent and incongruent).

2.3.8 Statistical Analysis

Normality was first assessed for each of the main outcomes using Kolmogorov-Smirnov and Shapiro-Wilk Tests, Skewness and Kurtosis values, as well as visual examination of Normal Q-Q Plots and histograms. Outliers were defined as values ±3 standard deviations from the mean and were removed from subsequent analyses (see **Figure 1**). To examine the relevance of IIV for behavioral performance, Pearson correlations were used to assess the relationships between SDRT and CVRT with accuracy and reaction time in both congruent and incongruent trials. Pearson correlations were also used initially to assess bivariate relationships between adiposity, cognitive measures, and fitness and demographic variables including BMI, age, pubertal timing, sex, and SES (2-tailed $p<0.05$ considered significant). Hierarchical linear regression analyses were performed to examine variability in cognitive performance. The demographic and IQ variables that were significant in the bivariate correlations were entered into Step 1. Steps 2 and 3 were used for VO_2FF and %fat, respectively, in the models where they correlated in the bivariate analysis. Each predictor was evaluated by studying its significance (α-level, 0.05). Finally, one-way ANOVA were used to determine differences in IIV across weight status grouping utilizing a 2 (type: congruent, incongruent) × 3 (group: healthy weight, overweight, obese) factorial model. Post hoc analyses included independent samples T-tests with Bonferroni correction. All analyses were completed using SPSS Version 24 (IBM, Armonk, NY).

2.4 Results

Preadolescent children ages 7 to 9 (N=314) were recruited from the east-central Illinois region. See **Figure 1** for consort diagram. The complete breakdown of demographics, body composition, and cognitive performance can be found in **Table 1**. SES categorization of the participants was 40% low, 36% middle, and 25% high. According to the Tanner pubertal staging questionnaire, 51% of participants were stage 1, 45% were stage 2, and 5% were stage 3. Categorizations for BMI showed 56% of the children were classed as healthy weight, 19% as overweight, and 23% as obese.

Table 2 shows the results of the bivariate correlations. For the congruent trials, correlations with SDRT showed a negative relationship with accuracy ($r=-0.27$ $p<0.01$) and a positive relationship with reaction time ($r=0.63$, $p<0.01$); and correlations with CVRT similarly showed a negative relationship with accuracy ($r=-0.51$, $p<0.01$). For the incongruent trials, SDRT was negatively correlated with accuracy ($r=-0.28$, $p<0.01$) and positively associated with reaction time ($r=0.54$, $p<0.01$), and CVRT was negatively associated with accuracy ($r=-0.59$, $p<0.01$) but not associated with reaction time. Overall results (i.e., collapsed across congruency) indicated that flanker SDRT was significantly correlated with age ($r=-0.230$, $p<0.01$), SES ($r=-0.15$, $p<0.05$), IQ ($r=-0.23$, $p<0.01$), and VO2FF ($r=-0.16$, $p<0.05$). Additionally, CVRT was correlated with age ($r=-0.25$, $p<0.01$), IQ ($r=-0.23$, $p<0.01$), VO_2FF ($r=-0.19$, $p<0.01$), and %fat ($r=0.20$, $p<0.01$).

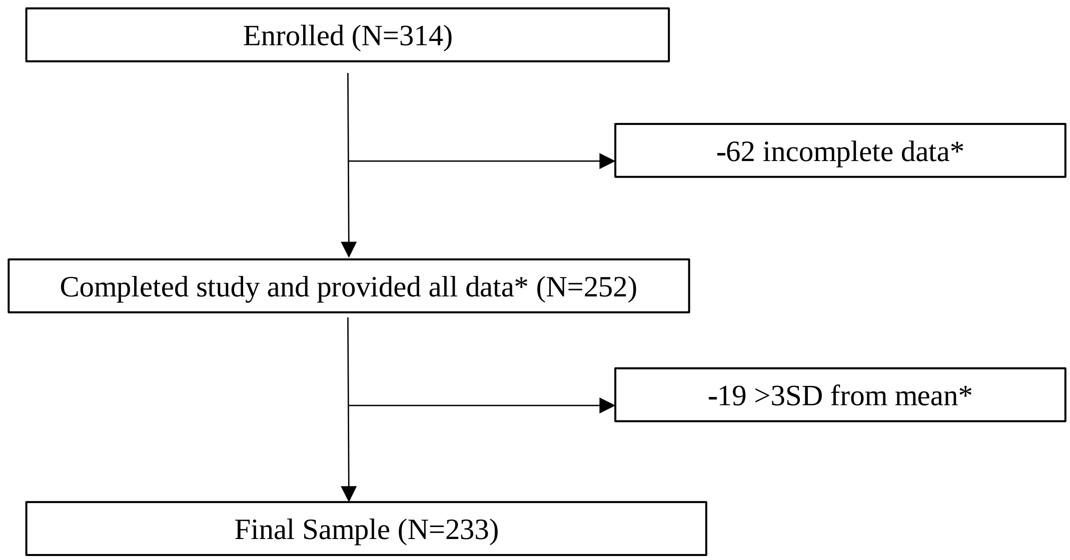
Results of the ANOVA can be seen in **Figure 2**. Results showed a significant effect of weight status in CVRT for both congruent [$F\ (3, 229) = 4.46$, $p<0.01$, $\eta^2=0.06$] and incongruent [$F\ (3, 229) = 6.77$, $p<0.01$, $\eta^2=0.08$] trials, with the healthy weight group exhibiting lower variability compared to both overweight and obese groups. Post hoc comparisons using the Bonferroni test indicated that both congruent ($p<0.02$) and incongruent ($p<0.01$) trials of CVRT were lower in healthy weight individuals than in individuals with obesity.

Hierarchical regression results are summarized in **Table 3** and **Table 4**. Whole-body adiposity was a significant predictor of congruent accuracy ($\beta=-0.15$, $p=0.02$), reaction time ($\beta=-0.14$, $p=0.03$), and CVRT ($\beta=0.15$, $p=0.02$), as well as incongruent CVRT ($\beta=0.15$, $p=0.02$).

VO_2FF was not a significant predictor of variance in any of the final models (all p's>0.05). Age, IQ, VO_2FF, and %fat explained 15% of the variance in congruent CVRT ($\Delta R^2=0.15$, F=10.24, p<0.01). Age, SES, VO_2FF, and %fat accounted for 18% of the variance in incongruent CVRT ($\Delta R^2=0.18$, F=9.70, p<0.01).

2.4.1 Figures and Tables

Figure 1: Consort Diagram



*All data includes values for age, sex, SES, IQ, Tanner, BMI, $VO_2peakFF$, %Fat, Flanker Compatible Congruent and Incongruent RT, %accuracy, SDRT, and CVRT.

Table 1: Demographics, IQ, Adiposity, and Flanker Performance

N=233		Mean (SD)
Age, y		8.67 (0.54)
Sex		
	Male	42.9% (n=100)
	Female	57.1% (n=133)
SES		
	Low	39.5% (n=92)
	Medium	35.6% (n=83)
	High	24.9% (n=58)
IQ		108.41 (12.92)
Pubertal Timing		1.36 (0.47)
BMI, kg/m2		18.83 (4.00)
Weight Status		
	Underweight	2.6% (n=6)
	Healthy Weight	56.2% (n=131)
	Overweight	18.5% (n=43)
	Obese	22.7% (n=53)
VO_2peak Relative		42.13 (7.20)
VO_2peak %tile		36.6 (30.40)
VO_2FF		61.00 (7.26)
%Fat		31.62 (6.88)
Flanker Congruent		
	Accuracy, %	80.26 (12.01)
	Reaction Time, ms	552.35 (103.62)
	SDRT, ms	182.43 (52.23)
	CVRT	0.33 (0.08)
Flanker Incongruent		
	Accuracy, %	72.93 (13.57)
	Reaction Time, ms	600.54 (113.64)
	SDRT, ms	193.84 (56.28)
	CVRT	0.32 (0.08)

Data presented as mean ± STD unless otherwise indicated

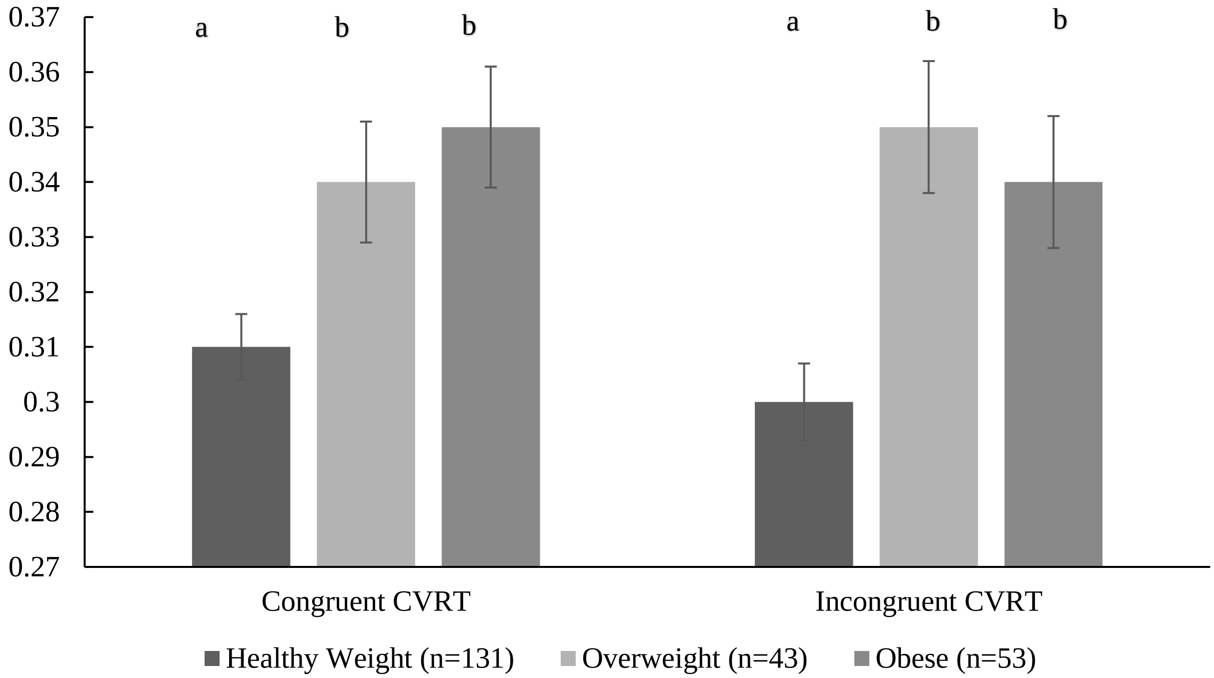
SES, Socioeconomic Status; IQ, Intelligence Quotient; BMI, Body Mass Index; VO_2peak %tile, Maximum Aerobic Capacity Age and Sex Percentile; VO_2FF, Maximum Lean Aerobic Capacity; %Fat, Whole Body Percent Fat; VAT, Visceral Adipose Tissue; SDRT, Standard Deviation of Reaction Time; CVRT, Coefficient of Variation of Reaction Time

Table 2: Bivariate Correlations Between Demographics, IQ, Weight Status, and Flanker Performance

		Congruent				Incongruent			
		Accuracy	RT	SDRT	CVRT	Accuracy	RT	SDRT	CVRT
	Age	0.25**	-0.19**	-0.27**	-0.22**	0.21**	-0.16*	-0.29**	-0.24**
	Sex	0.02	-0.01	-0.03	-0.02	0.01	-0.04	-0.14*	-0.10
	SES	0.12	-0.06	-0.08	-0.05	0.14*	-0.07	-0.19**	-0.17*
	IQ	0.24**	-0.06	-0.23**	-0.23**	0.26**	-0.04	-0.20**	-0.20**
	Pubertal Timing	-0.04	-0.13	-0.08	--0.00	-0.11	-0.12	-0.01	0.07
	BMI	-0.11	-0.19**	0.01	0.16*	-0.13*	-0.18**	0.03	0.18**
	VO_2FF	0.09	0.01	-0.10	-0.13*	0.15*	-0.03	-0.18**	-0.19**
	%Fat	-0.14*	-0.16*	0.02	0.16*	-0.14*	-0.13**	0.07	0.18**
Congr	SDRT	-0.27**	0.63**	-	-	-0.18**	0.54**	-	-
	CVRT	-0.51**	-0.00	-	-	-0.51**	-0.06	-	-
Incongr	SDRT	-0.34**	0.47**	-	-	-0.28**	0.54**	-	-
	CVRT	-0.59**	-0.13*	-	-	-0.59**	-0.11	-	-

** Correlation is significant at the 0.01 level (2-tailed)
*Correlation is significant at the 0.05 level (2-tailed)
SES, Socioeconomic Status; IQ, Intelligence Quotient; BMI, Body Mass Index; VO_2FF, Maximum Lean Aerobic Capacity; %Fat, Whole Body Percent Fat; SDRT, Standard Deviation of Reaction Time; CVRT, Coefficient of Variation of Reaction Time

Figure 2: Results of One-Way ANOVA for Differences in Coefficient of Variation Between Healthy Weight, Overweight, and Obese Individuals



Different letters depict significant difference between groups ($p<0.05$)

Table 3: Results for Hierarchical Regression for Congruent Flanker

Accuracy				Reaction Time				CVRT			
	β	R^2	F		β	R^2	F		β	R^2	F
Step 1		0.14**	19.36**	**Step 1**		0.04**	8.52**	**Step 1**		0.12**	16.17**
Age	0.30**			Age	-0.19**			Age	-0.27**		
IQ	0.29**							IQ	-0.28**		
Step 2		0.17**	15.20**	**Step 2**		0.06**	6.66**	**Step 2**		0.13**	11.46**
%Fat	-0.15*			%Fat	-0.14*			VO_2FF	-0.09		
								Step 3		0.15**	10.24**
								%Fat	0.15*		

**Significant at the 0.01 level (2-tailed)
*Significant at the 0.05 level (2-tailed)
†Marginally significant at the 0.10 level (2-tailed)
IQ, Intelligence Quotient; VO_2FF, Maximum Lean Aerobic Capacity; %Fat, Whole Body Percent Fat; CVRT, Coefficient of Variation of Reaction Time

Table 4: Results for Hierarchical Regression for Incongruent Flanker

Accuracy				Reaction Time				SDRT				CVRT			
	β	R^2	F		β	R^2	F		β	R^2	F		β	R^2	F
Step 1		0.14**	11.96**	**Step 1**		0.03*	6.36*	**Step 1**		0.19**	12.94**	**Step 1**		0.13**	11.79**
Age	0.25**			Age	-0.16*			Age	-0.33**			Age	-0.28**		
SES	0.07							Sex	-0.15*			SES	-0.11		
IQ	0.29**							SES	-0.12*			IQ	-0.23**		
								IQ	-0.24**						
Step 2		0.15**	9.66**	**Step 2**		0.04**	4.81**	**Step 2**		0.20**	11.07**	**Step 2**		0.15**	10.39**
VO_2FF	0.10			%Fat	-0.12†			VO_2FF	-0.11†			VO_2FF	-0.14*		
Step 3		0.16**										**Step 3**		0.18**	9.70**
%Fat	-0.12†		8.55**									%Fat	0.15*		

**Significant at the 0.01 level (2-tailed)
*Significant at the 0.05 level (2-tailed)
†Marginally significant at the 0.10 level (2-tailed)
SES, Socioeconomic Status; IQ, Intelligence Quotient; VO_2FF, Maximum Lean Aerobic Capacity; %Fat, Whole Body Percent Fat; SDRT, Standard Deviation of Reaction Time; CVRT, Coefficient of Variation of Reaction Time

2.5 Discussion

The use of IIV as a marker of cognitive impairment or dysfunction has been demonstrated in clinical studies among patients with brain disorders such as ADHD and Alzheimer's disease[123,124]. However, few have attempted to examine IIV in generalizable or non-clinical study populations, particularly in childhood. The results of the study were consistent with our *a priori* hypothesis given that we observed negative relationships between adiposity and task accuracy. Further, children with greater adiposity exhibited higher IIV indicating that the negative influence of excess fat mass extends to measures of dispersion in attentional inhibition, following adjustment for demographic factors, intelligence, and aerobic fitness. These findings were further supported by comparisons across weight status categories. Children with overweight and/or obesity exhibited greater IIV during both congruent and incongruent trials of the modified flanker task, relative to their healthy weight counterparts. Interestingly, differences across weight status categories were only evident for measures of IIV and not central tendency, providing further evidence supporting the susceptibility of measures of dispersion to the potentially negative influence of childhood obesity.

Although previous studies have observed an inverse relationship between aerobic fitness and IIV, these studies did not consider %fat as a contributing factor[13]. The results here indicated that fitness significantly contributed to the variation in CVRT during the incongruent trials; however, the inclusion of %fat in the regression models appeared to have a moderating influence on the initial relationships observed for fitness. This moderating influence of %Fat indicates that excess adiposity exerts a considerable negative impact on cognitive control that mitigates some of the positive contribution of fitness to the cognitive measures. Alternatively, the sample studied was relatively homogeneous with regard to fitness, and was predominantly comprised of lower-fit children. Conducting similar analyses in a heterogeneous sample that includes a greater proportion of higher-fit children may reveal a positive influence of fitness, independent of adiposity. Future studies among children with varying levels of fitness are necessary to further confirm the findings observed here.

Emerging evidence indicates that behavioral and emotional problems are more common among children with obesity with the most frequently implicated psychosocial factors including externalizing (e.g., impulsivity) and internalizing (e.g., depression and anxiety) behaviors[125]. Further, obesity has been linked to poorer ability for cognitive control processes such as attention, memory, and inhibition[13]. In two systematic reviews, higher BMI was associated with poorer cognitive control performance; however, there was little consistency within and across the different domains of cognitive control[13]. The conflicting state of knowledge may be, at least in part, due to the metric of performance studied. Virtually all previous studies on obesity and children's cognitive and neuropsychological function have relied on central tendency measures with little known regarding the influence of behaviors and physiological health on IIV. To our knowledge, the current study is the first to examine the relationship between measures of intraindividual performance and adiposity among preadolescent children.

The findings of the current study provide support linking IIV in cognitive control performance to the interrelated health factors of aerobic fitness and adiposity. However, the mechanisms underlying this observation are not clear. One possibility may be differential trajectories of development or maturation in cognitive control across health factors. For example, considering factors beyond adiposity and fitness, we observed that age was a significant predictor of both IIV and central tendency. As children develop and mature, they exhibit improved performance in cognitive control tasks, displaying both higher response accuracy and shorter response times[46].

Similarly, IIV performance during cognitive control tasks also decreases throughout childhood and adolescence[63]. These findings show consistency that younger children exhibit higher variability during cognitive control tasks. Conversely, Myerson et al. observed that older adults (M=73.9 years) exhibited greater IIV in their RT than did younger adults (M=20.9 years)[126]. In the same study, the older adults also displayed longer RT than the younger adults[126]. Der and Deary found similar results in a study of 7130 adults participants, they found that reaction time increased throughout the adult age range and reaction time variability decreased in early adulthood but then increased throughout late adulthood[127]. Collectively, these investigations suggest that the IIV-age relationship follows a U-shaped curve throughout the lifespan with improvements through young adulthood and decrements through older adulthood. These studies provide initial support for the theory of a developmental mechanism contributing to the differences in IIV and the results in the current work show consistency that older children exhibited lower response variability.

Additional insights into the underpinnings of response variability can be gained from magnetic resonance imaging (MRI) studies. Previous studies demonstrate that variability indexes a demand for top-down cognitive control[67]. Further, patients with damage to the dorsolateral prefrontal cortex or the superior medial frontal cortex exhibited increases in IIV during a cognitive control task that required feature discrimination and integration[128]. Diffusion tensor imaging studies show that reduced performance variability reflects the maturation of white matter connectivity[129]. Tamnes et al. reported that irrespective of age, lower IIV was associated with higher fractional anisotropy, lower mean diffusivity, lower axial diffusivity, and lower radial diffusivity; all indicating that children (8-19-year-olds) with more mature white matter exhibit lower degrees of performance variability[129]. Additionally, increased BMI is associated with a global and distributed decrease in white matter microstructural integrity as well as detectable brain volume deficits in people with obesity, including atrophy in the frontal lobes, anterior cingulate gyrus, hippocampus, and thalamus, when compared to normal-weight subjects[130]. These findings indicate that obesity is associated with decrease brain volume, supporting the theory that brain structure and development contribute to response time variability.

Limitations to this study include the report of cross-sectional data rather than an intervention approach. The cross-sectional design yields the possibility that observed fitness and adiposity differences may have resulted from a combination of extraneous factors not accounted for in the present investigation such as diet, survey response bias, or preexisting health conditions and undiagnosed mental disorders. Additionally, data were not collected regarding the amount of time that preadolescent children had been exposed to overweight or obesity. Children who have had overweight/obesity longer may have further cognitive impairment and additional research will need to account for this factor. Further, it is possible that the relationship between fitness, adiposity, and IIV is bidirectional. Therefore, additional randomized controlled and longitudinal trials are needed to elucidate the influence of change in health factors (i.e., fitness and fatness) to changes in cognitive control, with the current work highlighting the importance of utilizing dispersion measures, rather than central tendency alone, as perhaps more sensitive markers of obesity-related decrements in cognitive control in children.

2.6 Conclusions

In conclusion, the current work is based on a large dataset comprising fitness, adiposity, and cognitive control data in preadolescent children. The findings point to the importance of maintaining healthy weight status in children for better cognitive control. They also indicate that increased adiposity, regardless of fitness level, exhibits a deleterious relationship with aspects of children's cognitive control. The association between adiposity and IIV points to the important influence of excess fat mass on markers of cognitive control, which may serve a developmental barrier and contribute to long-term decrements in cognitive function.

CHAPTER 3: FUTURE DIRECTIONS AND CONCLUSIONS

The results of the present research suggested an association of adiposity relative to cognitive function in preadolescent children whereas no significant influence of aerobic fitness level was observed. However, this only indicates correlation not causation. Future work needs to focus on the directionality of the relationship. For example, is overweight and obesity directly contributing to poorer cognitive function or does the poorer cognitive function influence behavioral factors or decision-making related to dietary choices that influence chronic adipose tissue accumulation. Additional studies are needed to examine whether changes in adiposity and aerobic fitness have complementary influences on cognitive function in children. Furthermore, the work here supports that both children with overweight and those with obesity perform at lower levels than children who are healthy weight. Future studies should examine the amount of time that a child spends with overweight or obesity and how that can influence cognitive control. Previous work has shown adults with overweight and obesity experience white matter density changes and increased levels of inflammatory markers in the blood[29,130]. It is important, therefore, to determine if the amount of time exposed to overweight/obesity may be more detrimental than the class of overweight/obesity itself.

The results of this study were consistent with our *a priori* hypothesis in that children with greater adiposity exhibited higher IIV supporting that the negative influence of excess fat mass extends to measures of dispersion in attentional inhibition even after adjustment for demographic factors, intelligence, and aerobic fitness. Additionally, children with overweight and/or obesity exhibited greater IIV during both congruent and incongruent trials of the modified flanker task relative to their healthy weight counterparts. Interestingly these differences were only evident for measures of IIV and not central tendency, providing further evidence supporting the susceptibility of measures of dispersion to the potentially negative influence of childhood obesity. IIV and central tendency are both important to study, and the goal here is to provide evidence that both should be studied together to form a more complete picture, rather than saying one is more important than the other. While IIV can provide predictive information about within-person fluctuations, central tendency provides useful metrics in evaluation of overall performance. As Jensen et al mentioned, both RT and SDRT are important to study as they reflect different processes that are independently correlated with cognitive processes, with RT reflecting the speed of information processing and SDRT reflecting the consistency in processing speed[59]. In evaluating the results herein, it seems that CVRT may be the more relevant measurement of IIV. While SDRT is a measurement of the fluctuation in reaction time within the individual, the CVRT takes both the fluctuation in reaction time and the reaction time into account. In this way, CVRT is a measurement that can encompass a little of both metrics – the IIV and the central tendency.

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APPENDIX A: PRE-PARTICIPATION HEALTH SCREENING

Pre-Participation Health Screening

Physical activity and fitness testing are safe for most children. To ensure safe participation for your child we would like to know some specific information about your child's health before we include them in this study. In some cases, we simply need to know more information (e.g., that you child has a puffer for asthma) while in other situations, we might tell you that we'd like your child to see a physician before participating in the study. Please tick "☐ Yes" beside all items that apply to your child, and feel free to ask us to clarify if anything is unclear.

YES	NO	
☐	☐	1. Your child has a diagnosed medical condition that prevents them from participating in intense exercise.
☐	☐	2. A doctor has ever told you that it would be unsafe for your child to do intense exercise.
☐	☐	3. Anyone in your child's family has ever died of a sudden heart attack before the age of 35 years.
☐	☐	4. Anyone in your child's family has ever been diagnosed with a serious heart condition before the age of 35 years.
☐	☐	5. Your child has high blood pressure.
☐	☐	6. Your child has asthma and uses a puffer or inhaler.
☐	☐	7. Your child has diabetes.
☐	☐	8. Your child has epilepsy (seizures).
☐	☐	9. Your child has unexplained fainting or dizziness, especially with activity.
☐	☐	10. Your child has unexplained **chest pain**, breathlessness, or tiredness with activity.

Pre-Participation Health Screening (Dr. Mark Tremblay, University of Ottawa)

APPENDIX B: HEALTH HISTORY AND DEMOGRAPHICS SURVEY

Health History & Demographics Questionnaire

Please answer the following questions to the best of your ability.

General Information

1. What was your child's date of birth? _________/_________/_________

2. Was your child born before 37 weeks of pregnancy? ☐ Yes ☐ No

3. At what week of pregnancy was your child born? __________ weeks

4. What was your child's birth weight? __________lbs __________oz

5. Did the mother of your child suffer from any medical condition while she was pregnant? ☐ Yes ☐ No If yes, what condition?

6. What is your child's current age? _______________

7. What is your child's current (or recently completed) Grade Level? _______________

8. What is your child's sex? ☐ Male ☐ Female

9. Which is your child's dominant hand? ☐ Right ☐ Left ☐No Preference

10. Is your child color blind? ☐ Yes ☐ No

11. Does your child wear contacts or glasses? ☐ Yes ☐ No

    If yes, what was their prescription for?

Demographics

1. Does your child live with their biological parents? ☐ Yes ☐ No

2. Does your child live in a single parent/guardian household? ☐ Yes ☐ No

3. Does your child live with their Mother or a Female guardian? ☐ Yes ☐ No

4. Does your child's Mother/Female guardian work? ☐ Yes ☐ No
5. What is the highest level of education obtained by your child's Mother/Female guardian?
   a) Did not complete high school
   b) High School Graduate
   c) Some College
   d) Bachelor Degree
   e) Advanced Degree

6. Does your child live with their Father or a Male guardian? ☐ Yes ☐ No

7. Does your child's Father/Male guardian work? ☐ Yes ☐ No
8. What is the highest level of education obtained by your child's Father/Male guardian?
   a) Did not complete high school
   b) High School Graduate
   c) Some College
   d) Bachelor Degree
   e) Advanced Degree

9. How many other children (under the age of 18) live with your child? _______________
   How old are they? _______________
   What is their sex? _______________
10. How many biological siblings does your child have? _______________

11. Does your child receive free or reduced-price school lunch? ☐ Yes ☐ No

12. Do you consider yourself to be Hispanic or Latino (*A person of Mexican, Puerto Rican, Cuban, South or Central American, or other Spanish culture or origin, regardless of race*)? ☐ Yes ☐ No

13. What race / ethnicity do you consider your child?
    - a) American Indian or Alaska Native
    - b) Asian
    - c) Black or African American
    - d) Native Hawaiian or other Pacific Islander
    - e) White or Caucasian
    - f) Mixed or Other

14. What is your approximate household income?
    - a) <10,000
    - b) 10,000-20,000
    - c) 21,000-30,000
    - d) 31,000-40,000
    - e) 41,000-50,000
    - f) 51,000-60,000
    - g) 61,000-70,000
    - h) 71,000-80,000
    - i) 81,000-90,000
    - j) 91,000-100,000
    - k) 100,000+

Activities

1. Does your child participate in musical activities? ☐ Yes ☐ No

   If yes:

   Does your child play an instrument? ☐ Yes ☐ No

   If so, what instrument(s)?

   Does your child participate in choir? ☐ Yes ☐ No

   How many hours a week does your child spend participating in musical activities?

2. Does your child participate in religious activities? ☐ Yes ☐ No

   If yes, how many hours a week does your child spend participating in religious activities?

3. Does your child participate in sports activities? ☐ Yes ☐ No

   If yes:

   Does your child participate in formal youth sports? ☐ Yes ☐ No

   In what activities does your child participate?

4. Has your child attended regular afterschool care outside of your home in the last year? ☐ Yes ☐ No

Habits

1. How much time does your child spend watching <u>television</u> on an average day during the <u>week</u>?

   a) < 1 Hour per Day
   b) 1 to 2 Hours per Day
   c) 2 to 3 Hours per Day
   d) 3 to 4 Hours per Day
   e) 4 to 5 Hours per Day
   f) 5 to 6 Hours per Day
   g) 6 to 7 Hours per Day
   h) 7 to 8 Hours per day
   i) > 8 Hours per Day

2. How much time does your child spend watching <u>television</u> on an average day during the <u>weekend</u>?

   a) < 1 Hour per Day
   b) 1 to 2 Hours per Day
   c) 2 to 3 Hours per Day
   d) 3 to 4 Hours per Day
   e) 4 to 5 Hours per Day
   f) 5 to 6 Hours per Day
   g) 6 to 7 Hours per Day
   h) 7 to 8 Hours per day
   i) > 8 Hours per Day

3. How much time does your child spend on a <u>computer</u> on an average day during the <u>week</u>?

   a) < 1 Hour per Day
   b) 1 to 2 Hours per Day
   c) 2 to 3 Hours per Day
   d) 3 to 4 Hours per Day
   e) 4 to 5 Hours per Day
   f) 5 to 6 Hours per Day
   g) 6 to 7 Hours per Day
   h) 7 to 8 Hours per day
   i) > 8 Hours per Day

4. How much time does your child spend on a <u>computer</u> on an average day during the <u>weekend</u>?

   a) < 1 Hour per Day
   b) 1 to 2 Hours per Day
   c) 2 to 3 Hours per Day
   d) 3 to 4 Hours per Day
   e) 4 to 5 Hours per Day
   f) 5 to 6 Hours per Day
   g) 6 to 7 Hours per Day
   h) 7 to 8 Hours per day
   i) > 8 Hours per Day

5. How much time does your child spend playing <u>video games</u> on an average during the <u>week</u>?

   a) < 1 Hour per Day
   b) 1 to 2 Hours per Day
   c) 2 to 3 Hours per Day
   d) 3 to 4 Hours per Day
   e) 4 to 5 Hours per Day
   f) 5 to 6 Hours per Day
   g) 6 to 7 Hours per Day
   h) 7 to 8 Hours per day
   i) > 8 Hours per Day

6. How much time does your child spend playing <u>video games</u> on an average during the <u>weekend</u>?

   a) < 1 Hour per Day
   b) 1 to 2 Hours per Day
   c) 2 to 3 Hours per Day
   f) 5 to 6 Hours per Day
   g) 6 to 7 Hours per Day
   h) 7 to 8 Hours per day

d) 3 to 4 Hours per Day
j) >8 hours per day
e) 4 to 5 Hours per Day

7. How much time does your child spend being physically active on an average during the week?
   a) < 1 Hour per Day
   b) 1 to 2 Hours per Day
   c) 2 to 3 Hours per Day
   d) 3 to 4 Hours per Day
   e) 4 to 5 Hours per Day
   f) 5 to 6 Hours per Day
   g) 6 to 7 Hours per Day
   h) 7 to 8 Hours per day
   i) > 8 Hours per Day

8. How much time does your child spend being physically active on an average during the weekend?
   a) < 1 Hour per Day
   b) 1 to 2 Hours per Day
   c) 2 to 3 Hours per Day
   d) 3 to 4 Hours per Day
   e) 4 to 5 Hours per Day
   f) 5 to 6 Hours per Day
   g) 6 to 7 Hours per Day
   h) 7 to 8 Hours per day
   i) > 8 Hours per Day

9. How much sleep does your child regularly get?
   a) < 5 Hours per Day
   b) 5 to 6 Hours per Day
   c) 6 to 7 Hours per Day
   d) 7 to 8 Hours per Day
   e) 8 to 9 Hours per Day
   f) 9 to 10 Hours per Day
   g) > 10 Hours per Day

10. How much sleep did your child get last night?
   a) < 5 Hours
   b) 5 to 6 Hours
   c) 6 to 7 Hours
   d) 7 to 8 Hours
   e) 8 to 9 Hours
   f) 9 to 10 Hours
   g) > 10 Hours

11. How many caffeinated soft drinks does your child regularly drink in a day?

   ☐ None ☐ One ☐ Two ☐ Three or more

12. How many cups of tea does your child regularly drink in a day?

   ☐ None ☐ One ☐ Two ☐ Three or more

13. How often would you rate your child's stress level as HIGH?

   ☐ Occasionally ☐ Frequently ☐ Constantly

When was the last time your child:

Had a caffeinated substance?

Ate a meal or a snack?

What did s/he have to eat?

Exercised?

What type of exercise?

How long did s/he exercise for?

How intense did s/he work out?

General Health

1. When was the last time your child saw a doctor? ______________________
2. Does your child have any allergies? □ Yes □ No
3. Does your child have any food allergies? □ Yes □ No ____________________
   Is your child allergic to milk? □ Yes □ No
   Is your child allergic to soy? □ Yes □ No
   Please list any other allergies your child may have:____________________________

4. Is your child allowed to consume foods that contain animal products?
   □ Yes □ No (my child follows a strictly plant-based/vegan diet)
5. Was your child breastfed? □ Yes □ No
   If yes, what was the duration of exclusive (no formula at all) breast feeding? _____ months
   At what age did your child stop drinking **any** breast milk? ____months

6. At what age was infant formula introduced to your child? ________months

7. How old was your child when he/she was first fed something (e.g., cereals, pureed foods, solid foods) other than breast milk or formula? _______ months
8. Has your child ever been diagnosed with dyslexia? □ Yes □ No
9. Has your child ever been diagnosed with an attentional disorder? □ Yes □ No

10. Has your child ever been diagnosed with asthma? ☐ Yes ☐ No

11. Is your child epileptic? ☐ Yes ☐ No

12. Is your child diabetic? ☐ Yes ☐ No

If so please explain:

13. Has your child been diagnosed with any kind of cancer? ☐ Yes ☐ No
If so please explain:

14. Does your child have hearing loss or wear a hearing aid? ☐ Yes ☐ No

15. Has your child been hospitalized within the last 6 months? ☐ Yes ☐ No
If so please explain:

16. Has your child ever lost consciousness as a result of hitting their head? ☐ Yes ☐ No

If yes:

When did this occur?

Where did s/he hit his/her head?

How long was s/he unconscious?

17. Has your child ever lost consciousness as a result of any other type of injury or seizure? ☐ Yes ☐ No

If yes:

When did this occur?

How long was s/he unconscious?

Medications/Supplements

Medications: Is your child presently taking or have they taken any of the following medications within the past two months? Please circle your answer.

Asprin, Bufferin, Anacin	Tranquilizers
Blood Pressure pills	Weight reducing pills
Cortisone	Blood thinning pills
Cough Medicine	Dilantin
Digitalis	Allergy Shots
Hormones	Water pills
Insulin or Diabetic pills	Antibiotics
Iron or poor blood medications	Barbiturates
Laxatives	Phenobarbital
Sleeping pills	Thyroid medicine

Other(s):____

1. Does your child take Ginkgo Biloba supplements? ☐ Yes ☐ No

   If yes:

   When was the last time they took the supplement?

   What dose of the supplement did they take?

2. Does your child take Iron supplements? ☐ Yes ☐ No

   If yes:

   When was the last time they took the supplement?

   What dose of the supplement did they take?

3. Does your child take any stimulants or sedatives? ☐ Yes ☐ No

   If yes:

   What do they take?

   When was the last time they took it?

   What dose of it did they take?

Cardiovascular Health

Does your child have any of the following:

1. □ Yes □ No Pain or discomfort in the chest, neck, jaw, arms, or other areas that may be related to poor circulation.
2. □ Yes □ No Heartbeats or palpitations that feel more frequent or forceful than usual or feeling that your heart is beating very rapidly.
3. □ Yes □ No Unusual dizziness or fainting.
4. □ Yes □ No Shortness of breath while lying flat or a sudden difficulty in breathing that wakes them up while sleeping.
5. □ Yes □ No Shortness of breath at rest or with mild exertion (such as walking two blocks).
6. □ Yes □ No Feeling lame or pain in the legs brought on by walking.
7. □ Yes □ No A known heart murmur.
8. □ Yes □ No Unusual fatigue with usual activities.
9. □ Yes □ No Has any **male** in your immediate family had a heart attack or sudden death before the age of 55?
10. □ Yes □ No Has any **female** in your immediate family had a heart attack or sudden death before the age of 65?
11. □ Yes □ No Do you have family history of heart disease?
12. □ Yes □ No Do you have family history of lung disease?
13. □ Yes □ No Do you have family history of diabetes?
14. □ Yes □ No Do you have family history of strokes?
15. □ Yes □ No Has your child been diagnosed with a past or present cardiovascular disease?
16. □ Yes □ No Does your child have any significant heart rhythm disorder?
17. □ Yes □ No Has your child been diagnosed with hypertension?
18. □ Yes □ No Has your child been diagnosed with peripheral vascular disease?

Other
Is there anything else you feel we should know about your child's current/past health?

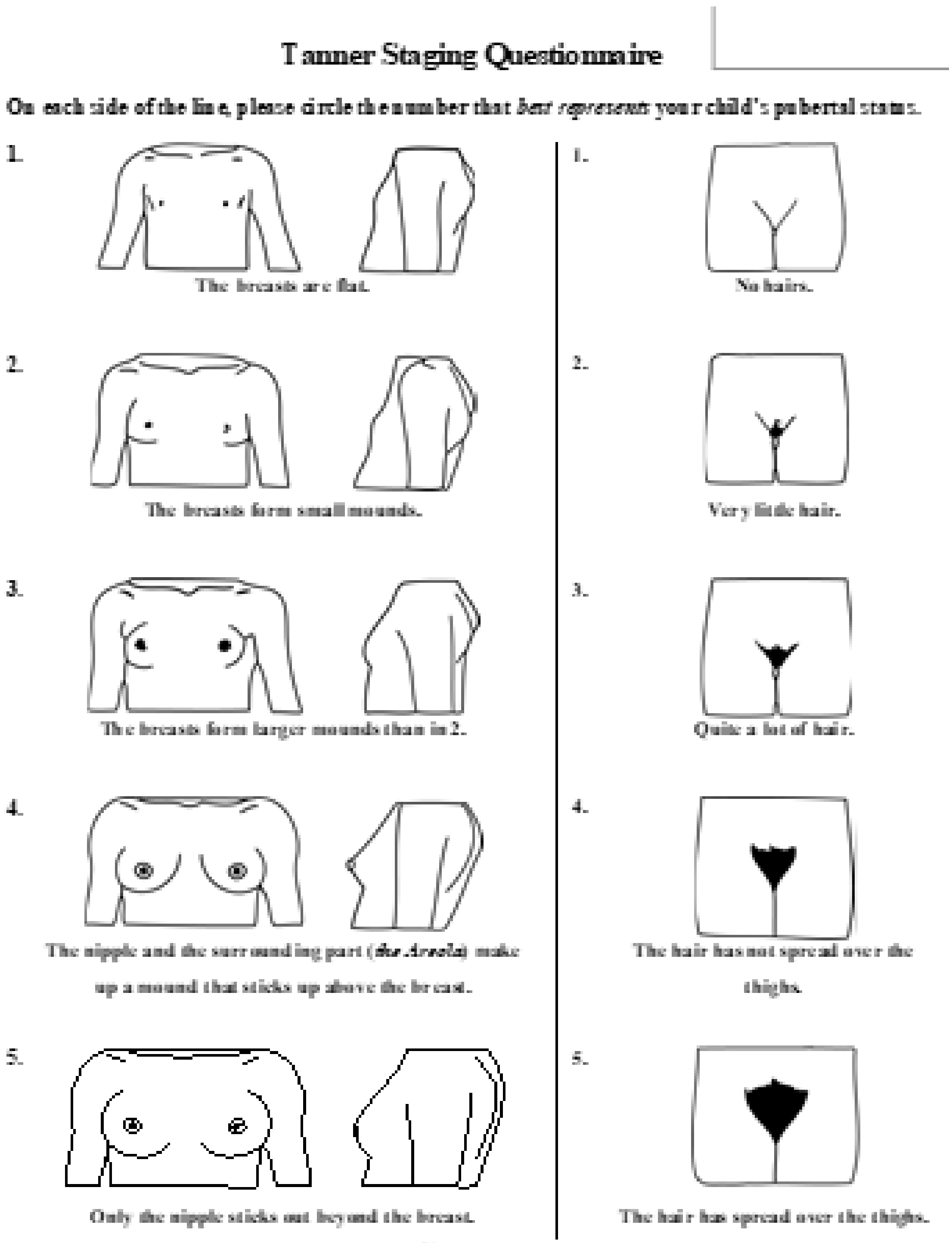
APPENDIX C: ADHD QUESTIONNAIRE

Please circle the number that *best describes* your child's home behavior over the last 6 months.

		Never or Rarely	Sometimes	Often	Very Often
1.	Fails to give close attention to details or makes careless mistakes in schoolwork.	0	1	2	3
2.	Fidgets with hands or feet or squirms in seat.	0	1	2	3
3.	Has difficulty sustaining attention in tasks or play activities.	0	1	2	3
4.	Leaves seat in situations in which remaining seated is expected.	0	1	2	3
5.	Does not seem to listen when spoken to directly.	0	1	2	3
6.	Runs about or climbs excessively in situations in which it is inappropriate.	0	1	2	3
7.	Does not follow through on instructions and fails to finish work.	0	1	2	3
8.	Has difficulty playing or engaging in leisure activities quietly.	0	1	2	3
9.	Has difficulty organizing tasks and activities.	0	1	2	3
10.	Is "on the go" or acts as if "driven by a motor."	0	1	2	3
11.	Avoids tasks (e.g. homework) that require sustained mental effort.	0	1	2	3
12.	Talks excessively.	0	1	2	3
13.	Loses things necessary for tasks or activities.	0	1	2	3
14.	Blurts out answers before questions have been completed.	0	1	2	3
15.	Is easily distracted.	0	1	2	3
16.	Has difficulty awaiting turn.	0	1	2	3
17.	Is forgetful in daily activities.	0	1	2	3
18.	Interrupts or intrudes on others.	0	1	2	3

DuPaul, Power, Anastopoulos, & Raid (1998).

APPENDIX D: TANNER PUBERTAL TIMING QUESTIONNAIRE



Tanner Staging Questionnaire

On each side of the line, please circle the number that *best represents* your child's pubertal status.

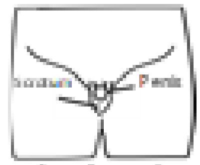
1. The breasts are flat.
2. The breasts form small mounds.
3. The breasts form larger mounds than in 2.
4. The nipple and the surrounding part (*the Areola*) make up a mound that sticks up above the breast.
5. Only the nipple sticks out beyond the breast.

1. No hairs.
2. Very little hair.
3. Quite a lot of hair.
4. The hair has not spread over the thighs.
5. The hair has spread over the thighs.

Tanner Staging Questionnaire

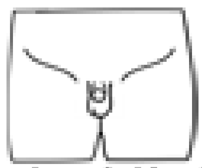
On each side of the line, please circle the number that *best represents* your child's pubertal status.

1.



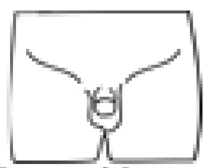
Scrotum and penis are the same size.

2.



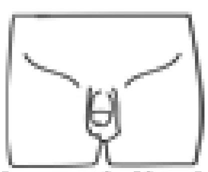
The scrotum has lowered a bit and the penis is a little larger.

3.



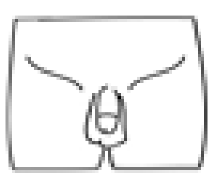
The penis is longer and the scrotum is larger.

4.



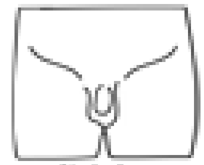
The penis is longer and wider; the scrotum is darker and bigger than before.

5.



The penis and scrotum are the size and shape of an adult.

1.

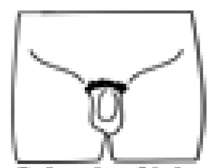


No hairs.

2.

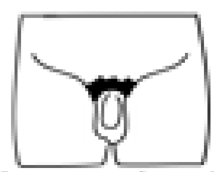
Very little hair.

3.



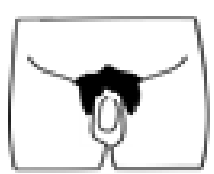
Quite a lot of hair.

4.



The hair has not spread over the thighs.

5.



The hair has spread over the thighs.