TRANSIENT MODULATIONS OF INHIBITORY CONTROL IN CHILDREN WITH ADHD:
THE EFFECT OF A SINGLE BOUT OF PHYSICAL ACTIVITY

BY

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DISSERTATION

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Abstract

Given the increasing prevalence of sedentary behaviors during childhood, and the concomitant pervasiveness of neurobehavioral disorders such as attention-deficit/hyperactivity disorder (ADHD), a greater understanding of the extent to which physical activity relates to brain health and cognition during development is of increasing importance. Accordingly, the aim of this investigation was to examine the effect of a single bout of moderately- intense aerobic exercise on preadolescent children with ADHD. Using a within-participants design, event-related potentials and task performance were assessed while participants performed an interference control task following a bout of exercise or seated reading during two separate, counterbalanced sessions. Following a single bout of exercise, both children with ADHD and healthy match-control children exhibited greater response accuracy and enhanced stimulus-related processing, with ADHD children also exhibiting selective enhancements in regulatory processes, relative to after a similar duration of seated reading. Enhanced scholastic performance in the areas of Reading and Arithmetic were also observed following exercise for both children with ADHD and healthy match-control children. These findings indicate that single bouts of moderately-intense aerobic exercise may serve as a transient non-pharmaceutical treatment option for children with ADHD to improve the cognitive health, academic performance, and overall effective functioning of this population.

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Chapter 1

Introduction

Attention-deficit/hyperactivity disorder (ADHD) has become one of the most prevalent childhood disorders in the United States affecting over 2.5 million children (American Psychiatric Association, 2000; Biederman, 1998; Wolraich, Hannah, Baumgaertel, & Feurer, 1998). This neurobehavioral disorder is characterized by developmentally inappropriate levels of inattention, over-activity, distractibility, and impulsiveness, which manifests during childhood (American Psychiatric Association, 2000; Banaschewski et al., 2006; Scharchar, Mota, Logan, Tannock, & Klim, 2000). However, research suggests that failures in inhibition may represent the core cognitive deficit underlying the manifestation of ADHD (Barkley, 1997). Although pharmacological treatments have largely been found effective in the short-term management of behavioral symptoms (Solanto, Arnsten, & Castellanos, 2001), concerns over the long-term implications of psychostimulant use have led a push for alternative, non-pharmaceutical treatment options for children with ADHD (Wilson & Jennings, 1996). One such option may be single bouts of short-duration, moderately intense aerobic exercise. Anecdotal reports from parents, teachers, and scholars have suggested that single bouts of aerobic activity may benefit children with ADHD (Panksepp, 2007; Tantillo, Kesick, Hynd, & Dishman, 2002). Yet, a paucity of empirical evidence exists in this population. However, previous research in healthy children and young adults has suggested that a single bout of aerobic exercise is beneficial for a variety of cognitive functions (Lambourne & Tomporowski, 2010), with a disproportionately larger benefit for inhibitory aspects of cognitive control (Brisswalter, Collardeau, & Arcelin, 2002; Hillman, Snook, & Jerome, 2003, Hillman, Pontifex et al., 2009; Hogervorst, Riedel,

Jeukendrup, & Jolles, 1996; Lichtman & Poser, 1983; Sibley, Etnier, & LeMasurier, 2006; Tomporowski, 2003a, 2003b).

Cognitive control describes an overarching set of higher-order cognitive operations, which are involved in the regulation of goal-directed interactions within the environment (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Meyer & Keiras, 1997; Norman & Shallice, 1986). These processes allow for the optimization of behavior through the selection, scheduling, coordination, and maintenance of computational processes that underlie aspects of perception, memory, and action (Botvinick et al., 2001; Meyer & Keiras, 1997; Miyake, Friedman, Emerson, Witzki, & Howerter, 2000; Norman & Shallice, 1986). The core cognitive processes, which collectively comprise what is termed 'cognitive control', include inhibition, working memory, and cognitive flexibility (Diamond, 2006). In developing populations, inhibition is particularly important to cognitive operations as it allows for sustained attention and maintenance of control over one's actions (Diamond, 2006). Thus, inhibitory control allows for one to deliberately override a dominant response in order to perform a less potent but correct response, suppress task irrelevant information in the stimulus environment, and override an ongoing response (Barkley, 1997; Davidson, Amso, Anderson, & Diamond, 2006).

Of the core cognitive control processes, deficits in inhibition have consistently been observed (via decreased response accuracy, and longer and more variable reaction time [RT]) in previous investigations into ADHD across a variety of tasks (e.g., flanker, Go/No-Go, Stroop; Albrecht et al., 2008; Booth, Carlson, & Tucker, 2007; Castellanos et al., 2000; Crone, Jennings, & van der Molen, 2003; Hartung, Milich, Lynam, & Martin, 2002; Iaboni, Douglas, & Baker, 1995; Jonkman et al., 1999; Konrad, Neufang, Hanisch, Fink, & Herpertz-Dahlmann, 2006; Scheres et al., 2004; Vaidya et al., 1998, 2005; van Meel, Heslenfeld, Oosterlan, & Sergeant,

2007; Yong-Liang et al., 2000). Findings from a number of meta-analysis have observed moderate effect sizes for ADHD-related deficits of inhibitory control ranging from 0.54 to 0.75 (Homack & Riccio, 2004; Pennington & Ozonoff, 1996; Willcut, Doyle, Nigg, Faraone, & Pennington, 2005). Collectively, these findings provide converging evidence to support the conclusion that inhibitory aspects of cognitive control are impaired in ADHD.

Interestingly, investigations into the effects of acute exercise on behavioral indices of cognitive control in healthy young adults have predominately-utilized tasks that tap aspects of inhibition (i.e., flanker, Stroop, and the Paced Auditory Serial Addition Test; Hillman et al., 2003; Hogervorst et al., 1996; Kamijo, Nishihira, Higashiura, & Kuroiwa, 2007; Lichtman & Poser, 1983; Sibley et al., 2006; Tomporowski et al., 2005). Findings from these investigations have observed that a single 20 to 40 minute bout of aerobic physical activity at an intensity between 60 and 85% of maximal heart rate resulted in facilitations in general aspects of cognition, with a selectively larger increase in performance for task components requiring larger inhibitory control demands (Hogervorst et al., 1996; Kamijo et al., 2007; Lichtman & Poser, 1983; Sibley et al., 2006; Tomporowski et al., 2005). Although substantially less research has examined the effects of a single bout of physical activity in healthy children, findings from these investigations are consonant with previous research into the effects of acute exercise on cognition in adult populations. That is, following participation in a single bout of structured physical activities lasting at least 20 minutes, improvements in cognition have been observed for both simple and choice RT tasks (Ellemberg & St-Louis-Deschênes, 2010), aspects of concentration (Caterino & Polak, 1999; Mahar et al., 2006; McNaughten & Gabbard, 1993) and mathematics (Gabbard & Barton, 1979), brief tests of academic achievement (Hillman, Pontifex et al., 2009), and inhibitory control (Hillman, Pontifex et al., 2009).

Despite these seemingly disparate bodies of literature, there is striking similarity between the aspects of cognition that are influenced by acute exercise and those that exhibit ADHD related deficits. However, to date, no prior research has investigated the influence of a single bout of physical activity on inhibitory aspects of cognitive control in children with ADHD. Some evidence to suggest that physical activity may be beneficial to children with ADHD is provided by Taylor, Kuo, and Sullivan (2001), who found a reduction in parent-reported ADHD-related symptoms following exposure to environmental settings conducive to physically active behaviors (e.g., parks, backyards, and neighborhoods) relative to urban settings (e.g., parking lots, downtown areas, and indoors). Thus, this investigation suggests that physically active behaviors may provide a transient, non-pharmaceutical treatment option for children with ADHD.

A more precise understanding of the relationship between acute exercise and ADHD may be provided through the assessment of event-related brain potentials (ERPs). ERPs refer to a class of neuroelectric activity that occurs in response to, or in preparation for, a stimulus or response; and provide a means of gaining insight into a subset of covert processes that occur between stimulus encoding and response production (Coles, Gratton, & Fabiani, 1990). One such ERP component, which occurs in response to a stimulus, is the fronto-central N2. The amplitude of the fronto-central N2 is believed to reflect response inhibition (Schmitt, Münte, & Kutas, 2000) associated with conflict monitoring processes during correct trials in a manner similar to that proposed for the ERN discussed below (Ridderinkhof et al., 2002; van Veen & Carter, 2002; Yeung, Cohen, & Botvinick, 2004), while the latency of the fronto-central N2 is thought to reflect aspects of the response selection process (Gajewski, Stoerig, & Falkenstein, 2008). Distinct from the N2, the amplitude of the P3 component has been related to the allocation of attentional resources (Polich, 1987; Polich & Heine, 1996), while the latency of the P3 is thought

to index stimulus classification and evaluation speed, independent of response selection and action (Duncan-Johnson, 1981; Verleger, 1997). A separate ERP component that occurs following errors of commission is the error-related negativity (ERN; also known as the Ne). The ERN is thought to reflect activation of action monitoring processes in response to erroneous behaviors in order to initiate the upregulation of top-down compensatory processes regardless of an individual's awareness of the error (Falkenstein, Hohnsbein, Hoormann, & Blanke, 1991; Gehring & Knight, 2000; Gehring, Goss, Coles, Meyer, & Donchin, 1993; Nieuwenhuis, Ridderinkhof, Blom, Band, & Kok, 2001).

Previous examinations of children with ADHD using neuroelectric measures have begun to elucidate a number of deficient neurocognitive processes. Specifically, children with ADHD, relative to healthy controls, exhibit reductions in the amplitude of the fronto-central N2 (Albrecht et al., 2008; Barry, Johnstone, & Clarke, 2003; Dimoska, Johnstone, Barry, & Clarke, 2003; Johnstone & Barry, 1996; Liotti et al., 2007; Pliszka, Liotti, & Woldorff, 2000; Wiersema, van der Meere, Roeyers, Coster, & Baeyens, 2006), smaller P3 amplitude (Barry et al., 2003; Jonkman et al., 1999, 2000; Kemner et al., 1996; Liotti et al., 2007; Loiselle, Stamm, Maitinsky, & Whipple, 1980; Wiersema et al., 2006), longer P3 latency (Barry et al., 2003; Jonkman et al., 1999), and smaller ERN amplitude (Albrecht et al., 2008; Liotti, Pliszka, Perez, Kothmann, & Woldorff, 2005; van Meel et al., 2007) across a variety of tasks. Such a pattern of findings suggest that deficits in the cascade of processes underlying the stimulus-response relationship; including reductions in response inhibition (N2 amplitude), the allocation of attentional resources (P3 amplitude) and the speed in which stimuli are processed (P3 latency), and failures to appropriately implement action monitoring processes (ERN amplitude), may underlie ADHD-related deficits in inhibitory control.

With regard to acute exercise, little research has utilized neuroelectric measures to examine the effects of a single bout of physical activity on inhibitory aspects of cognitive control, with only a single study examining a preadolescent population (Hillman, Pontifex et al., 2009). However, findings in children and college age young adults have suggested that a 20-30 minute bout of moderate-intensity aerobic exercise increases the allocation of attentional resources (as indexed by an enhancement of the amplitude of the P3 ERP component), and facilitates cognitive processing and stimulus classification speed (as indexed by a decrease in the latency of the P3 ERP component), with a disproportionately larger effect for task conditions requiring greater inhibitory control demands (Hillman et al., 2003; Hillman, Pontifex et al., 2009; Kamijo et al., 2004, 2007, 2009). To date, only a single study has investigated the relationship between acute exercise and action monitoring processes in college-aged young adults, and observed no exercise-induced modulations in the ERN ERP component (Themanson & Hillman, 2006). Thus, additional research is needed in order to better understand the relationship between acute exercise and action monitoring processes.

One means of investigating action monitoring processes is through the utilization of task conditions that modulate the demands on cognitive control. That is, previous research in young adults has observed an upregulation of action monitoring processes as a function of task instructions stressing accuracy over speed (Gehring et al., 1993). However, preadolescent children exhibit a tendency to respond with greater impulsivity and variability in RT than adults, suggesting that this population may be unable to modulate response strategies via instruction (Davidson et al., 2006). Accordingly, previous investigations have suggested that the modulation of action monitoring processes may be achieved in preadolescent children by manipulating stimulus-response compatibility characteristics of a modified flanker task to create multiple

gradations of stimulus and response configurations, allowing for the modulation of inhibitory control requirements (Friedman, Nessler, Cycowicz, & Horton, 2009; Pontifex et al., 2011).

Thus, the purpose of this study was to examine the effect of a single bout of moderate intensity aerobic exercise on the modulation of inhibitory control deficits using a task that elicits multiple levels of conflict in children with ADHD. Given that a single bout of aerobic exercise exerts a positive effect over the same aspects of cognition in which children with ADHD exhibit deficits; it was hypothesized that acute exercise would result in a reduction of ADHD-related deficits in task performance, P3 amplitude, and P3 latency with selectively larger effects for task conditions requiring greater amounts of cognitive control. Such a pattern of findings would suggest that a single bout of aerobic exercise ameliorates ADHD-related deficits in inhibitory control function through an increase in the allocation of attentional resources and faster stimulus classification and processing speed. Alternatively, based on previous acute exercise findings (Hillman, Pontifex et al., 2009; Themanson & Hillman, 2006), no exercise induced changes in N2 or ERN amplitude were hypothesized, suggesting that a single bout of aerobic exercise does not exert an effect over response conflict or action monitoring processes. Thus, the current investigation may provide additional insight into the nature of ADHD-related deficits in cognitive control and indicate that acute exercise may serve as a transient non-pharmaceutical treatment option for children with ADHD to increase the cognitive health and effective functioning of this population.

Chapter 2

Review of Literature

To better understand why a single bout of aerobic exercise may serve to modulate ADHD-related deficits in cognitive control, it is necessary to review the existing literature on ADHD, cognitive control, neuroelectric indices of cognition, and acute exercise. First, a theoretical overview of ADHD, its proposed subtypes, and its relationship to cognitive control will be discussed to provide a framework for understanding this participant population. Second, the literature on single bouts of physical activity will be reviewed to elucidate the beneficial influences of acute exercise on aspects of cognitive control. Finally, the existing literature on both ADHD and acute exercise on neuroelectric indices of cognitive processes will be examined to provide justifications for the present investigation.

Attention Deficit-Hyperactivity Disorder

ADHD is the most prevalent neurobehavioral disorder of childhood in the United States (American Academy of Pediatrics, 2000), affecting approximately 5-15% of school aged children (American Psychiatric Association, 2000; Biederman, 1998; Wolraich et al., 1998), with approximately 30-50% of clinically diagnosed cases persisting into adulthood (Barkley, Fischer, Edelbrock, & Smallish, 1990; Klein & Mannuzza, 1991; Weiss, Hechtman, & Weiss, 1999). According to the National Institutes of Health (NIH), this neurobehavioral disorder resulted in over $3 billion in expenses to the public school systems in the United States in 1995 alone (NIH, 1998). Over the course of development, ADHD is associated with increased risks for poorer academic achievement and peer/family relations, disciplinary problems in and out of school, early substance experimentation and abuse, anxiety, depression, aggression, and later in life difficulties in adult social/romantic relationships and maintaining employment (Barkley,

Guevremont, Anastopoulos, DuPaul, & Shelton, 1993; Booth et al., 2007; Bracken & Boatwright, 2005). ADHD is defined by developmentally malapropos levels of inattention, over-activity, distractibility, and impulsiveness manifesting as a childhood-onset disorder (American Psychiatric Association, 2000; Banaschewski et al., 2006; Scharchar et al., 2000).

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR; American Psychiatric Association, 2000) ADHD refers to the diagnostic entity encompassing three subtypes of ADHD: predominately inattentive (ADHD-I), predominately hyperactive/impulsive (ADHD-H), and combined inattentive/hyperactive/impulsive (ADHD-C). According to Applegate and colleagues (1997), the predominately hyperactive/impulsive (ADHD-H) subgroup is typically observed among preschool children, as the hyperactive-impulsive behavior pattern seems to first emerge during the preschool years, and only accounts for approximately 10% of children with ADHD (American Academy of Pediatrics and National Initiative for Children's Healthcare Quality, 2002). Symptoms of inattention appear to have later onsets with ADHD-I and ADHD-C predominately occurring during the school-aged years (Hart, Lahey, Loeber, Applegate, & Frick, 1995; Loeber, Green, Lahey, Christ, & Frick, 1992). The ADHD-I subgroup (formerly classified as attention-deficit disorder [ADD]) is characterized by developmentally inappropriate behaviors such as failing to attend and follow directions, having difficulty sustaining attention and organizing activities, and being easily distracted and forgetful (Barkley, DuPaul, & McMurray, 1990; Bracken & Boatwright, 2005). Further, the ADHD-I subgroup has been found to have a higher prevalence rate among girls (American Academy of Pediatrics and National Initiative for Children's Healthcare Quality, 2002). According to Barkley (1997), despite differences in symptomology between ADHD subtypes, they appear to share a central deficit related to cognitive control dysfunction, and in particular failures of inhibitory

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control (Barkley, 1997; Geurts, Verté, Oosterlaan, Roeyers, & Sergeant, 2005; Schachar & Logan, 1990).

Cognitive Control

The term cognitive control (also referred to as 'executive control') describes an overarching set of higher-order, cognitive operations, which are involved in the regulation of goal-directed interactions within the environment (Botvinick et al., 2001; Meyer & Keiras, 1997; Norman & Shallice, 1986). These processes allow for the optimization of behavior through the selection, scheduling, coordination, and maintenance of computational processes underlying aspects of perception, memory, and action (Botvinick et al., 2001; Meyer & Keiras, 1997; Miyake et al., 2000; Norman & Shallice, 1986). The core cognitive processes which are collectively termed 'cognitive control' include inhibition, working memory, and cognitive flexibility (Diamond, 2006). Of these core processes, inhibition has been the most studied in the acute exercise literature (e.g., Hillman et al., 2003; Hillman, Pontifex et al., 2009; Kamijo et al., 2004, 2007) and relates to the ability to act on the basis of choice rather than impulse (Davidson et al., 2006). That is, inhibitory control often requires one to deliberately override a dominant response in order to perform a less potent but correct response, suppress task irrelevant information in the stimulus environment, or stop an ongoing response (Barkley, 1997; Davidson et al., 2006). This ability to inhibit attention to task irrelevant or distracting stimuli is central to the ability to sustain attention and allow control over one's actions. Further, these abilities are particularly important to the effective functioning of cognitive control (Barkley, 1997; Brocki & Brohlin, 2004), and exhibit protracted development relative to other cognitive processes (Diamond, 2006).

One model of cognitive control which has been proposed is the dual mechanisms of cognitive control model (Braver, Gray, & Burgess, 2007) which suggests that the adaptability of the cognitive control system is achieved through two dissociable subsystems of control referred to as 'proactive' and 'reactive' (Braver et al., 2007). These systems are distinguished by the time course in which behavior modifications occur; with proactive control modifying interactions in the environment prior to stimulus engagement (i.e., early selection) and reactive control occurring in direct response to the demands of an event (i.e., late correction; Jacoby, Kelley, & McElree, 1999). That is, proactive cognitive control, which neuroimaging research suggest is likely rooted in the dorsolateral prefrontal cortex (DLPFC; Braver et al., 2007; MacDonald, Cohen, Stenger, & Carter, 2000), works to continually exert top-down control in preparation for and during ongoing information processing allowing for flexible, online adjustments of attention (Braver et al., 2007; Botvinick et al., 2001). These alterations in attention serve to facilitate optimal completion of a task by providing enhanced maintenance of task demands and stimulus representations (Botvinick et al., 2001). This active maintenance comes at a cost however; as it requires extended periods of high levels of neuronal activity (in areas such as the lateral PFC) resulting in a larger metabolic demands (Braver et al., 2007). In contrast, reactive cognitive control, which neuroimaging research suggests is likely rooted in the anterior cingulate cortex (ACC), is transiently engaged following the occurrence of some imperative event and serves to initiate the activation of compensatory adjustments in top-down control in order to resolve conflict, increase response strength, or correct an impending error (Braver et al., 2007; Botvinick et al., 2001). However, reactive cognitive control represents a suboptimal control strategy which may be more susceptible to stimulus-based interference and may be insufficient when stimulus processing is constrained (Braver et al., 2007). Taken together, these 'proactive' and 'reactive'

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cognitive control mechanisms interact to optimize behavioral interactions within the environment (MacDonald et al., 2000).

One paradigm often used to elicit cognitive control, known as the Eriksen flanker task (Eriksen & Eriksen, 1974), employs multiple gradations of stimulus and response configurations requiring the modulation of inhibition for successful performance. This paradigm is conceptually simplistic in that it requires the discrimination of a centrally presented target stimulus amid lateral flanking stimuli, and has been utilized with a variety of stimuli (e.g. letters, arrows, fish; Eriksen & Schultz, 1979; Hillman et al., 2003; Ridderinkhof, van der Molen, Band, & Bashore, 1997; Rueda et al., 2004) and participant populations (e.g., children, young adults, older adults, athletes with a history of mild traumatic brain injury; Friedman et al., 2009; Pontifex et al., 2010, 2011; Pontifex, O'Connor, Broglio, & Hillman, 2009) indicating that children as young as 4 years can successfully complete this task (Mezzacappa, 2004). In this task, perceptually-induced response interference can be evoked by manipulating the compatibility of the target and flanking stimuli. In the congruent array (e.g., <<<<< or HHHHH), the target stimulus and the flanking stimuli are identical, resulting in faster and more accurate responses relative to the incongruent array (e.g., <<><< or HHSHH), where the target and flanking stimuli are mapped to opposing action-schemas (Eriksen & Schultz, 1979). The incongruent array results in the concurrent activation of both the correct response (elicited by the target) and the incorrect response (elicited by the flanking stimuli) before stimulus evaluation is complete; thus, requiring greater amounts of interference control to inhibit the flanking stimuli and execute the correct response (Spencer & Coles, 1999). Variants of this task have also manipulated the response characteristics of the target stimuli to require even greater levels of inhibitory control (Friedman et al., 2009; Pontifex et al., 2011). In these variants, participants first complete the standard flanker task described

above with the congruent and incongruent arrays to build-up a prepotent response mapping.

Next, an incompatible stimulus-response condition is performed, wherein the response mappings

to each of the stimuli are reversed (e.g., a target stimulus which previously required a left

response, now requires a right response). Thus, this condition necessitates the greatest amount of

inhibitory control among the four conditions (congruent-compatible, congruent-incompatible,

incongruent-compatible, incongruent-incompatible) to regulate the interference of the flanking

stimuli as well as inhibit the prepotent response-mapping (Friedman et al., 2009; Pontifex et al.,

2011).

Cognitive Control and ADHD

Previous investigations into the relationship of ADHD to cognitive control have

consistently observed deficits in inhibition. That is, within the flanker task, findings from a

number of investigations have observed decreased response accuracy (Albrecht et al., 2008;

Booth et al., 2007; Crone et al., 2003; Jonkman et al., 1999; Konrad et al., 2006; Scheres et al.,

2004; Vaidya et al., 2005; van Meel et al., 2007) as well as longer and more variable RT

(Albrecht et al., 2008; Booth et al., 2007; Crone et al., 2003; Jonkman et al., 1999) for children

with ADHD, relative to healthy match-controls. These findings of ADHD-related deficits in

cognition appear to be robust across a variety of inhibitory control tasks. For instance, the Stroop

task taps inhibitory aspects of cognitive control by requiring participants to inhibit the dominant

response tendency to read the color word and instead name the color of the ink in which the word

is printed (Homack & Riccio, 2004). Findings from meta-analyses of children with ADHD have

revealed moderate effect sizes ranging from 0.69 to 0.75 for ADHD-related deficits on the

condition of the Stroop task requiring inhibitory control (Homack & Riccio, 2004; Pennington &

Ozonoff, 1996). Similarly, investigations utilizing the Go/NoGo task, which taps inhibitory

aspects of cognitive control by developing a prepotent response during the Go condition, with the NoGo condition requiring response inhibition of the prepotent response, have consistently observed longer RT and increases in error rates for ADHD populations (Castellanos et al., 2000; Hartung et al., 2002; Iaboni et al., 1995; Trommer et al., 1988; Vaidya et al., 1998; Yong-Liang et al., 2000). Taken together, these findings provide converging evidence to support the conclusion that inhibitory aspects of cognitive control are impaired in ADHD. To date, within the limited body of research examining differences in inhibitory control as a function of ADHD subtype , there appears to be no difference between any of the three subtypes as measured through the flanker and Stroop tasks (Mullane, Corkum, Klein, & McLaughlin, 2009; Scheres et al., 2004). Further insight into these ADHD-related deficits in inhibitory control may be garnered from investigations utilizing structural and functional MRI, which have observed reduced tissue volume in the prefrontal cortex (Castellanos et al., 1996; Filipek et al., 1997; Giedd et al., 1994; Hynd et al., 1991; Yeo et al., 2003), the corpus callosum (Baumgardner et al., 1996; Giedd et al., 1994), and the basal ganglia (Aylward et al., 1996; Castellanos et al., 2001; Hynd et al., 1991; Rubia et al., 1999), in addition to decreased activation of the ACC in response to inhibitory control tasks for ADHD participants (Bush et al., 1999; Pliszka et al., 2006), suggesting that dysregultion of these brain structures may contribute to producing the core cognitive deficits of ADHD (Bush et al., 1999).

Physical Activity and ADHD

Thus far, pharmacological treatments using psychostimulants have been found effective in the short-term treatment of behavioral symptoms of ADHD (Solanto et al., 2001). However, concerns over the long term implications of psychostimulant use, including abuse and dependence, have yet to be adequately addressed (Moll, Hause, Ruther, Rothenberger &

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Huether, 2001; Wilson & Jennings, 1996). As a result, research suggests that parents are increasingly willing to investigate alternative treatments for ADHD, particularly those treatments that do not include medication administration (Wilson & Jennings, 1996). One such non-pharmaceutical treatment option for children with ADHD may be physical activity. Anecdotal reports from parents, teachers, and scholars have suggested that single bouts of physical activity may be beneficial to children with ADHD (Panksepp, 2007; Tantillo et al., 2002). Empirically, research utilizing animal models has observed that physical activity served to ameliorate impulsivity in rats lesioned to exhibit ADHD-like symptoms (Panksepp, Burgdorf, Turner, & Gordon, 2003). Although there is a tenuous link between artificially-induced ADHD-like symptoms in rats and ADHD in children, this investigation provides compelling evidence to suggest that physical activity may be beneficial to children with ADHD. Further evidence can be gleaned from Taylor , Kuo, and Sullivan (2001), who observed an amelioration of self-reported ADHD symptoms following exposure to environmental settings conducive to physically active behaviors (e.g., parks, backyards, and neighborhoods) relative to urban settings (e.g., parking lots, downtown areas, and indoors) in a sample of 96 preadolescent children with ADHD. Taken together, these findings provide converging evidence to suggest that physically active behaviors may provide a non-pharmaceutical treatment option for children with ADHD.

However, limited research has reported on the effect of a single bout of physical activity on cognition in children with ADHD (Craft, 1983), with no prior research focusing on inhibitory aspects of cognitive control. Craft (1983) was the first to empirically investigate the relationship between acute exercise and cognition in children with ADHD. Specifically, Craft (1983) utilized a sample of 31 ADHD and 31 healthy-match control boys between the ages of 7 and 10 years old to examine the effects of 1, 5, and 10 minutes of cycling on a stationary ergometer. Findings

revealed no differences in cognition, as measured by the Wechsler Intelligence Scale for Children – Revised (WISC-R) digit span and coding B or the Illinois Test of Psycholinguistic Abilities (ITPA) – visual sequential memory assessments, for either the ADHD or healthy control participants (Craft, 1983). Although children with ADHD exhibited decrements in performance for both tests of the WISC-R and the ITPA, the duration of the exercise bout may have been insufficient to alter cognition given that no acute exercise effects were observed for either participant group. Further, the exercise modality (i.e., cycling) may have been poorly chosen for this age group as preadolescent children have underdeveloped knee extensor muscles resulting in localized muscular fatigue and exhaustion following pedaling on a cycle (Bar-Or, 1983). Craft (1983) noted that the majority of participants exhibited signs of exhaustion at the 10 minute mark, providing additional support for this view.

Within the small body of research that has investigated the effects of a single bout of physical activity on healthy children; improvements in cognition have been observed for aspects of concentration (Caterino & Polak, 1999; Mahar et al., 2006; McNaughten & Gabbard, 1993) and mathematics (Gabbard & Barton, 1979), as well as shorter RT for both simple and choice RT tasks (Ellemberg & St-Louis-Deschênes, 2010) following participation in single bouts of structured physical activities lasting at least 20 minutes. These findings are consonant with previous research into the effects of acute exercise on cognition in adults, suggesting that a single bout of aerobic exercise positively influences a variety of cognitive functions (Brisswalter et al., 2002; Etnier et al., 1997; Lambourne & Tomporowski, 2010; Tomporowski, 2003b), with a disproportionately larger benefit for tasks or task components requiring greater cognitive control demands (Hillman et al., 2003; Hillman, Pontifex et al., 2009; Hogervorst et al., 1996; Lichtman & Poser, 1983; Sibley et al., 2006; Pontifex, Hillman, Fernhall, Thompson, & Valentini, 2009).

Investigations into acute exercise-induced changes in behavioral indices of cognitive control have predominately used tasks that tap aspects of inhibitory control (i.e., Stroop and the Paced Auditory Serial Addition Test), and have observed improvements in performance following at least 20 minutes of exercise (Hogervorst et al., 1996; Lichtman & Poser, 1983; Sibley et al., 2006; Tomporowski et al., 2005). Specifically, following an hour of aerobic exercise at 70% of maximal work capacity, Hogervorst et al. (1996) observed improved performance only on the color-word condition of the Stroop task, which requires the greatest amount of cognitive control, relative to the pre-exercise and baseline conditions. Similarly, both Sibley et al. (2006), and Lichtman & Poser (1983) observed general, yet selective effects on the Stroop task following 20 and 40 minutes of moderate intensity aerobic exercise, respectively. Further support for the beneficial effects of acute exercise on inhibitory aspects of cognitive control have been garnered from Tomporowski et al. (2005), who observed facilitations in performance on the Paced Auditory Serial Addition Test following a 40 minute bout of moderate intensity aerobic exercise. Collectively, the findings from these investigations suggest that changes in cognition following acute exercise may be selectively larger for aspects of cognitive control.

Extending these previous investigations, recent findings by Pontifex, Hillman, Fernhall and colleagues (2009) observed that exercise-induced modulations in cognitive control may be selective to aerobic exercise. Specifically, shorter RT on a Sternberg working memory task was observed immediately and 30 minutes following a 30 minute bout of moderate intensity aerobic exercise, with a disproportionately larger reduction in RT for task conditions placing the greatest demands upon working memory (Pontifex, Hillman, Fernhall et al., 2009). These findings were not observed following a 30 minute bout of resistance training (anaerobic exercise condition) or

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seated rest. Accordingly, the results of these investigations indicate that brief bouts of moderate intensity aerobic exercise relate to facilitations in behavioral indices of cognitive control processes.

Event-Related Brain Potentials

Beyond the assessment of overt actions, event-related brain potentials (ERPs) provide a means of gaining insight into the relationship between single bouts of aerobic exercise and cognitive control through the examination of a subset of processes that occur between stimulus encoding and response production. Accordingly, these measures allow for a more precise understanding of the effects of acute exercise on changes in cognition. ERPs refer to a class of neuroelectric activity that occurs in response to, or in preparation for, a stimulus or response (Coles et al., 1990). This neuroelectric activity is reflective of the synchronous activity of large populations of neurons (Hugdahl, 1995), and can reflect obligatory responses (exogenous) and higher-order cognitive processing that often require active participation from the subject (endogenous; Hugdahl, 1995). The stimulus-locked ERP is characterized by a succession of positive (P) and negative (N) components, which are constructed according to their direction and the relative time that they occur (Hruby & Marsalek, 2003). Earlier components (N1, P2) of the stimulus-locked potential relate to aspects of selective attention, while later components (N2, P3) relate to various aspects of endogenous cognitive function (e.g., response inhibition, attentional resource allocation).

> **N2.**

The fronto-central N2 (also known as the N200, control-related N2, and the conflict N2) is a negative going deflection that peaks approximately 180 to 350 milliseconds after stimulus onset, with a topographic maximum over fronto-central recording sites (Folstein & Van Petten,

2008; Patel & Azzam, 2005). The amplitude of the N2 is believed to reflect response inhibition (Falkenstein, Hoormann, & Hohnsbein, 1999; Schmitt et al., 2000) associated with conflict monitoring processes during correct trials, such that larger N2 amplitude is associated with increased conflict (Ridderinkhof et al., 2002; van Veen & Carter, 2002; Yeung et al., 2004). While the latency of the N2 ERP component is thought to reflect aspects of the response selection process (Gajewski et al., 2008). The neural tissue underlying the generation of the fronto-central N2 has been localized to midline frontal cortical areas, in particular the anterior cingulate cortex (ACC), through a number of hemodynamic and high-density dipole modeling localization studies (Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004; van Veen & Carter, 2002). Given that the fronto-central N2 and the response locked ERN component (discuss below) have been localized to the ACC, a number of researchers have posited that the N2 and ERN may reflect similar conflict-related processes (van Veen & Carter, 2002; Yeung et al., 2004).

P3.

Among ERP components, the P3 (also known as the P300 or P3b) has garnered considerable attention in the literature in regards to the effects of acute exercise on changes in cognition. Originally discovered in 1965 by Sutton, Braren, Zubin, and John; the P3 is a positive going deflection occurring approximately 300 to 800 milliseconds after stimulus presentation, with a topographic maximum at electrode sites over the parietal cortex (Polich & Kok, 1995). This endogenous component reflects neuronal activity associated with the revision of the mental representation of the previous event (Donchin, 1981), such that the P3 is sensitive to the allocation of attentional resources during stimulus engagement (Polich, 2007). Accordingly, based on a recent theoretical account of the P3 by Polich (2007), the amplitude is believed to be proportional to the resources allocated towards the suppression of extraneous neuronal activity in

order to facilitate attentional processing. P3 latency is generally considered as a measure of stimulus detection and evaluation time (Ilan & Polich, 1999; Magliero, Bashore, Coles, & Donchin, 1984), which is independent of response selection and behavioral action (Verleger, 1997). Further, P3 latency appears to be negatively correlated with mental function, with shorter latencies related to superior cognitive performance (Emmerson, Dustman, Shearer, & Turner, 1989; Howard & Polich, 1985; Johnson, Pfefferbaum, & Kopell, 1985; Polich & Martin, 1992; Polich, Howard, & Starr, 1983). Although the precise neural origins of the P3 are still unknown, the generation of the P3 appears to result from the interaction between frontal and temporal/parietal networks with additional contributions stemming from a number of subcortical structures (Ebmeier et al., 1995; Kirino, Belger, Goldman-Rakic, & McCarthy, 2000; Polich, 2003).

Error-Related Negativity (ERN).

Another class of ERPs is time-locked to an individual's response. One such ERP component is the error-related negativity (ERN; also known as the Ne), a negative going deflection occurring approximately 50 to 150 milliseconds after errors of commission with a topographic maximum over fronto-central recording sites (Falkenstein et al., 1991; Gehring et al., 1993). The ERN is thought to reflect the activation of action monitoring processes in response to erroneous behaviors to initiate the upregulation of top-down compensatory processes to correct an individual's responses during subsequent environmental interaction (Falkenstein et al., 1991; Gehring & Knight, 2000; Gehring et al., 1993). Further, the ERN occurs regardless of an individual's awareness of error commission (Nieuwenhuis et al., 2001). The neural tissue underlying the generation of the ERN has been localized through hemodynamic (Carter et al., 1998), magneto-encephalographic (Miltner et al., 2003), and high-density dipole modeling

(Dehaene, Posner, & Tucker, 1994; van Veen & Carter, 2002) studies to the dorsal portion of the ACC.

Event-Related Brain Potentials and ADHD

Findings from neuroelectric investigations of children with ADHD have predominately observed deficits in a number of neurocognitive processes. In particular, converging evidence across a variety of tasks suggest that children with ADHD exhibit deficits in: response inhibition as indexed by reductions in the fronto-central N2 (Barry et al., 2003; Dimoska et al., 2003; Johnstone & Barry, 1996; Liotti et al., 2007; Pliszka et al., 2000; Wiersema et al., 2006), the allocation of attentional resources as indexed by reductions in P3 amplitude (Barry et al., 2003; Jonkman et al., 2000; Kemner et al., 1996; Liotti et al., 2007; Loiselle et al., 1980; Wiersema et al., 2006), stimulus classification and processing speed as indexed by longer P3 latency (Barry et al., 2003), and action monitoring processes as indexed by reductions in the ERN component (Liotti et al., 2005). Consistent findings have been observed from investigations examining ADHD related deficits in neuroelectric indices of cognitive control in response to the flanker task (Albrecht, et al., 2008; Jonkman et al., 1999; van Meel et al., 2007). That is, in samples of preadolescent children with ADHD, relative to healthy controls, participants exhibit reductions in the amplitude of the fronto-central N2 (Albrecht et al., 2008), smaller P3 amplitude and longer P3 latency (Jonkman et al., 1999), and smaller ERN amplitude (Albrecht et al., 2008; van Meel et al., 2007). Taken together, these findings suggest that children with ADHD may exhibit decreased task performance on the flanker task as a result of deficient response inhibition, allocation of attentional resources and stimulus processing, and failures to appropriately implement action monitoring processes. Limited research exists examining ADHD subtype differences in neuroelectric components. However, Holcombe, Ackerman, and Dykman (1985)

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provides some preliminary evidence to suggest that deficits in P3 latency may be shared by both ADHD-I and ADHD-C subtypes, while reduced P3 amplitude may be specific to ADHD-I subtypes in response to perceptual discrimination tasks. Conservatively however, Baeyens, Roeyers, and Walle (2006) note that the lack of consistent differentiation between ADHD subtypes on neurophysiological measures reflects the similarity between subtypes with varying degrees of deviation from normal development.

The Effects of Single Bouts of Exercise on Event-Related Brain Potentials

To date, only a handful of previous investigations have examined the effect of brief bouts of aerobic exercise on neuroelectric indices of cognitive control. Findings from these investigations have largely been positive, suggesting benefits to neurocognitive processes following the cessation of a single bout of exercise (Hillman et al., 2003; Hillman, Pontifex et al., 2009; Kamijo et al., 2004, 2007, 2009). Both Hillman et al. (2003) and Kamijo et al. (2007) separately investigated the effect of acute aerobic exercise on the P3-ERP component in college-aged young adults in response to a modified Eriksen flanker task (Eriksen & Eriksen, 1974). Replicating the findings of Hillman et al. (2003), Kamijo et al. (2007) observed that after moderate intensity aerobic exercise, participants' exhibited larger P3 amplitudes across task conditions with selectively shorter P3 latencies observed for incongruent trials, which require the greatest amount of cognitive control to manage flanker-related interference. These findings (Hillman et al., 2003; Kamijo et al., 2007) indicate that in college-aged young adults, single bouts of moderate intensity aerobic exercise influence neuroelectric processes underlying cognitive control through the increased allocation of attentional resources and changes in cognitive processing and stimulus classification speed. Additional support for the beneficial effects of acute exercise on neurocognitive processes have been garnered from other research

employing a different cognitive control task. Specifically, Kamijo et al. (2004) examined the influence of a single bout of aerobic exercise on the P3-ERP component in college-aged young adults in response to a Go/NoGo task, which manipulates the need for response inhibition. Findings revealed that following an acute bout of moderate intensity aerobic exercise, larger P3 amplitude was observed for both the Go and NoGo conditions, suggesting that acute exercise may relate to general improvements in the allocation of neuroelectric resources involved in attention and inhibition (Kamijo et al., 2004).

Acute Exercise, Cognition, and Preadolescent Children

Although the majority of research on acute exercise and cognition has focused on adult populations, a more recent focus has been on pediatric populations. Reviews of early behavioral studies testing this relationship suggest that school age children also may derive cognitive benefits from physical activity participation (Sibley & Etnier, 2003; Tomporowski, 2003a). Accordingly, Hillman, Pontifex et al. (2009) assessed the extent to which improvements in cognition following a single bout of moderate intensity aerobic exercise effect both basic (i.e., laboratory tests) and applied (i.e., scholastic performance) aspects of cognition in preadolescent children. Findings from this investigation revealed that following a single 20 minute bout of moderately-intense treadmill walking, relative to seated rest, children exhibited improved response accuracy in response to a modified flanker task, had selectively larger P3 amplitudes for incongruent trials, and better performance on the Wide Range Achievement Test — 3rd edition (Hillman, Pontifex et al., 2009). Collectively, these findings indicate a positive effect of single, acute bouts of moderately-intense aerobic exercise and inhibitory aspects of cognitive control, which appears to relate to alterations in attentional resource allocation, cognitive processing and stimulus classification speed, and scholastic performance.

Although the majority of previous investigations on acute exercise and neuroelectric indices of cognitive control have focused on the P3-ERP component, only a single study has investigated the effect of acute exercise and response-locked action monitoring processes as indexed by the ERN-ERP component. Themanson and Hillman (2006) examined action monitoring processes in response to a flanker task in a sample of college-aged young adults. Findings revealed no relationship between 30 minutes of moderate intensity aerobic exercise and neuroelectric indices of action monitoring (Themanson & Hillman, 2006). Thus, these findings suggest that acute exercise-induced changes in neuroelectric processes underlying cognitive control are selective to the allocation of attentional resources and appear to be unrelated to action monitoring processes. It is important to note however, that this investigation only assessed college-aged young adults who collectively were performing the flanker task at an accuracy level above 90%, which allowed for a relatively small number of error trials to include in ERN averages. Thus, further research is necessary to better understand single bout of exercise on action monitoring processes under conditions allowing for a greater number of errors to achieve a more robust index of the neuroelectric indices underlying action monitoring. Additional research is needed to explore other participant populations to better understand the relationship between acute exercise and action monitoring processes. Accordingly, with the robust relationship between ADHD and reductions in the ERN component underlying action monitoring, this population may be primed to examine such an effect.

Purpose

Given that a single bout of aerobic exercise exerts a positive effect over the same aspects of cognition in which children with ADHD exhibit deficits; this proposal employed a neuroelectric perspective to examine the relationship between a single bout of moderately intense

aerobic exercise and children with ADHD. Specifically, this proposal sought to understand how ADHD-related deficits in neuroelectric indices of response inhibition, attentional resource allocation, cognitive processing and stimulus classification speed, and action monitoring processes may modulate as a function of acute exercise. Proper control groups (i.e., 'healthy', age-matched children) and conditions (i.e., seated reading) were implemented for comparison purposes. Accordingly, the examination of this relationship provides additional insight into the nature of ADHD-related deficits in cognitive control as well as the beneficial influence that physical activity has on processes related to cognitive function.

Rationale

Despite the growing body of research, the understanding of the relationship between single bouts of exercise and cognition remains incomplete, particularly as it relates to preadolescent populations. Thus, the present investigation provides insight into the flexible modulation of cognitive control processes and its relationship with acute exercise. Further, the nature of this relationship was examined in both "normal" prototypical preadolescent children and children with ADHD. If a significant relationship exists between acute exercise and cognitive control in children with ADHD, these findings may inform about transient non-pharmaceutical options for the treatment of ADHD, and would support the use of single bouts of exercise as a means for improving the cognitive health, academic performance, and overall effective functioning of this population.

Hypothesis

The first purpose of this investigation was to determine the effects of a single bout of aerobic exercise on behavioral and neuroelectric indices of cognition during performance of a

task requiring variable amounts of cognitive control in children with Attention-deficit/hyperactivity Disorder, r*elative to seated rest*. It was predicted that:

a. Participation in a single bout of aerobic exercise would result in more accurate task performance with a selectively larger effect for task conditions requiring greater amounts of cognitive control, indicating that aerobic exercise is beneficial to behavioral indices of cognitive function.

b. Participation in a single bout of aerobic exercise would result in an increase in the stimulus-locked P3 amplitude and shorter P3 latency, reflecting greater shifts in attention and processing speed. Selectively larger effects were predicted for task conditions requiring greater amount of cognitive control, indicating that a single bout of aerobic exercise is beneficial to neuroelectric indices of attention.

c. Participation in a single bout of aerobic exercise would result in no changes in the stimulus-locked N2 or response-locked ERN, indicating that acute exercise-induced changes in cognitive performance are specific to aspects of attention and processing speed.

The second purpose of this investigation was to determine the effects of a single bout of aerobic exercise on behavioral and neuroelectric indices of cognition during performance of a task requiring variable amounts of cognitive control in children with ADHD, r*elative to healthy match-control children*. It was predicted that:

a. At rest, differences in children with ADHD, relative to healthy match-control children, would manifest as less accurate performance, smaller N2 and P3 amplitudes, longer P3 latency, and reduced ERN amplitude, indicating impairments in inhibitory aspects of cognitive control.

b. Participation in a single bout of aerobic exercise would result in a reduction of

ADHD-related deficits in task performance and P3 amplitude and latency, such that

differences between groups would no longer be apparent.

Chapter 3

Methodology

The relationship between a single bout of aerobic exercise and modulations in cognitive control in children with ADHD was investigated. A sample of preadolescent children with ADHD and healthy match-control children were recruited from the East Central Illinois area. Each participant underwent neuroelectric and behavioral assessment during the completion of two conditions of a modified flanker task following 20 minutes of aerobic exercise and 20 minutes of reading.

Participants and Recruitment

A total of 20 ADHD (6 female) and 20 healthy match-control (6 female) preadolescent children between the ages of 8 and 10 from the East Central Illinois area were recruited to participate. ADHD participants were recruited from the general community population based on suspected or diagnosed attention deficit/hyperactivity disorder. Clinical status was verified through the ADHD supplement of the Kiddie-Sads-Present and Lifetime Version (K-SADS) semi-structured diagnostic interview using DSM-IV-TR criteria for any subtype of ADHD, including evidence for impairment in two or more settings and onset of symptoms before 7 years of age (American Psychiatric Association, 2000). Quantification of the clinical characteristics were assessed using the ADHD Rating Scale IV – Parent Version (DuPaul, Power, Anastopoulos, & Reid, 1998), the Child Behavioral Checklist – Parent Version (Achenbach & Rescorla, 2001), the Disruptive Behavior Rating Scale – Parent Version (Erford, 1993), and the Social Communication Questionnaire (Rutter, Bailey, & Lord, 2003). Children with ADHD scoring high on the oppositional defiance disorder (ODD) subscale of the Disruptive Behavior Rating Scale were retained given the high comorbidity between ADHD and ODD (Jenson,

Martin, & Cantwell, 1997). All participants provided written assent and their legal guardians provided written informed consent in accordance with the Institutional Review Board of the University of Illinois at Urbana-Champaign and Carle Foundation Hospital. All participants were administered the Kaufman Brief Intelligence Test (K-BIT; Kaufman & Kaufman, 1990) by a trained experimenter to assess intelligence quotient, and completed the Eidenburgh Handedness Inventory (Oldfield, 1971) to determine hand dominance. Socioeconomic status (SES) was determined using a trichotomous index based on: participation in free or reduced-price lunch program at school, the highest level of education obtained by the mother and father, and number of parents who worked full-time (Hillman et al., in press). Healthy match-control children were yoked by sex, age, pubertal status, and SES; which are factors known to influence cognitive function in this age group.

      Exclusionary criteria.

      Non-consent of the child or the child's guardian resulted in the participant being excluded from the investigation. Any participant outside of the 8-10 year old age range was not included as a result of individual differences in the onset of puberty and its effects on ERP measures (Davies, Segalowitz, & Gavin, 2004). That is, significant findings may be confounded by the fact that some of the participants may enter puberty at an earlier age than others, and the occurrence of this confound increases with age. To ensure that all study participants were in the earliest stages of puberty or have not yet begun pubertal changes, any participant with a score greater than 2 on the modified Tanner Staging Scales (Taylor et al., 2001) was excluded from the investigation. Any participant who was not capable of performing exercise based on the Physical Activity Readiness Questionnaire (PAR-Q; Thomas, Reading, & Shephard, 1992) and/or Health History & Demographics Questionnaire was excluded from the investigation for their safety.

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Similarly, all participants had normal or corrected to normal vision, and were free of any central

nervous system-active pharmacologic therapy for at least 1 month prior to testing. However, no

participant was taken off medication specifically for this investigation. All participants were

screened for autism spectrum disorders using the Social Communication Questionnaire with

scores above 15 resulting in exclusion (Rutter et al., 2003), and affective disorders (including

depressive and bipolar disorders), anxiety disorders, conduct disorders, and somatic disorders

using the Child Behavioral Checklist with DSM-oriented scores falling above the 97th percentile

resulting in exclusion (Achenbach & Rescorla, 2001). Children with ADHD were screened to

ensure that they were currently exhibiting ongoing ADHD symptoms as indicated by a score at

or above the 90th percentile on the ADHD Rating Scale-IV. Inclusionary criteria for all

participants, as well as specific inclusionary criteria for ADHD and healthy-control participants

are provided in Table 3.1.

Power Analysis

An *a priori* power analysis was conducted to estimate the appropriate sample size

necessary for detecting an effect of acute aerobic exercise on P3 amplitude given the inclusion of

potentially confounding variables (i.e., age, sex, IQ, and SES). An effect size was calculated

from the results reported in Hillman, Pontifex et al. (2009) for the effect of acute aerobic exercise

on P3 amplitude in healthy preadolescent children. Specifically, Hillman, Pontifex, and

colleagues (2009) observed increased P3 amplitude following acute exercise (M=8.6 µV,

SD=3.67) relative to rest (M=5.5 µV, SD=4.16) resulting in a moderate-to-large effect size

(Cohen's $d = 0.79$). To determine the appropriate sample size necessary for detecting differences

between children with ADHD and healthy match-controls in cognitive control tasks, a moderate

effect size (Cohen's $d = 0.54$) is provided by a recent meta-analysis conducted by Willcut et al.

(2005). Therefore, conservatively assuming the smaller effect size ($d = 0.54$), two-sided alpha of .05, and beta of .20 (i.e., 80% power), a sample size of 20 participants per group should yield a final sample size appropriate for adequate power.

Cognitive Control Task

Participants completed a modified version of the Eriksen flanker task (Eriksen & Eriksen, 1974) in which participants were instructed to respond as accurately as possible to the direction of a centrally presented target fish amid either congruous or incongruous flanking fish (see figure 3.1; Hillman et al., 2006; Pontifex & Hillman, 2007). The task also manipulated stimulus-response compatibility to vary cognitive control requirements by instructing participants to first complete a compatible condition (described above) and then complete an incompatible condition whereby participants were instructed to respond as quickly and accurately as possible in the direction opposite that of the centrally presented target arrow (Friedman et al., 2009; Pontifex et al., 2011). This task manipulated task difficulty through multiple levels of conflict (i.e., perceptual and response conflict) such that incongruent trials presented during the incompatible response condition should necessitate the greatest amount of inhibitory control. For each compatibility condition, two blocks of 100 trials were presented with equiprobable congruency and directionality. The stimuli were 3 cm tall yellow fish, which were presented focally for 200 ms on a blue background with a fixed inter-stimulus interval of 1700 ms. This task results in a number of behavioral performance indices of interest. In particular, primary analysis utilized reaction time (RT; i.e., time in ms from the presentation of the stimulus) and response accuracy (i.e., number of correct and error responses) measures in addition to interference score measures (incongruent – congruent). Additional mean response latencies were calculated within each participant for: 1) correct trials, 2) error trials, 3) matched-correct trials (the subset of correct

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trials matched to specific error trials based on RT), 4) correct trials following an error trial, and

5) correct trials following a matched-correct trial. Stimulus presentation, timing, and

measurement of behavioral response time and accuracy was controlled by Neuroscan Stim (v

2.0) software.

Neuroelectric Assessment

Electroencephalographic (EEG) activity was recorded from 64 sintered Ag-AgCl

electrode (10 mm) sites (FPz, Fz, FCz, Cz, CPz, Pz, POz, Oz, FP1/2, F7/5/3/1/2/4/6/8, FT7/8,

FC3/1/2/4, T7/8, C5/3/1/2/4/6, M1/2, TP7/8, CB1/2, P7/5/3/1/2/4/6/8, PO7/5/3/4/6/8, O1/2)

arranged in an extended montage based on the International 10-10 system (Chatrian, Lettich, &

Nelson, 1985) using a Neuroscan Quik-cap (Compumedics, Inc, Charlotte, NC). Recordings

were referenced to averaged mastoids (M1, M2), with AFz serving as the ground electrode, and

impedance less than 10kΩ. Additional electrodes were placed above and below the left orbit and

on the outer canthus of each eye to monitor electro-oculographic (EOG) activity with a bipolar

recording. Continuous raw EEG data was collected using Neuroscan Scan software (v 4.5)

through a Neuroscan Synamps 2 amplifier with a 24 bit A/D converter and +/- 200 millivolt

(mV) input range (763 µV/bit resolution) at a sampling rate of 500 Hz, amplified 500 times with

a DC to 70 Hz filter, and a 60 Hz notch filter. Continuous data was corrected offline for EOG

artifacts using a spatial filter (Compumedics Inc, Neuroscan, 2003). The spatial filter procedure

utilizes a spatial singular value decomposition (SVD) analysis that performs a Principle

Component Analysis (PCA) approach to determine the major components that characterize the

covariance matrix of the EOG artifact between all channels. This procedure then reconstructs all

of the original channels without the artifact components from the SVD analysis (Compumedics

Inc, Neuroscan, 2003).

Stimulus-locked epochs were created for correct trials from -100 to 1000 ms around the stimulus, baseline corrected using the -100 to 0 ms pre-stimulus period, and filtered using a zero phase shift low-pass filter at 30Hz (24 dB/octave). Additional screening for artifact in the EEG signal was conducted using a P3-screening procedure in which a 2 Hz half-sine wave template was shifted across a 300-700 ms window from the centro-parietal (CPz) and parietal electrode (Pz) sites to identify when a P3 was absent (Ford, White, Lim, & Pfefferbaum, 1994) or if an amplitude excursion of ± 75 µV occurred. Artifact-free data that were accompanied by correct responses were averaged. The N2 and P3 components were evaluated as the mean amplitude within a 50 ms interval surrounding the largest negative going peak within a 150 – 350 ms latency window and the largest positive going peak within a 300 – 700 ms latency window, respectively (Gamer & Berti, 2010; Sass et al., 2010). Amplitude was measured as the difference between the mean pre-stimulus baseline and mean peak-interval amplitude; peak latency was defined as the time point corresponding to the maximum peak amplitude.

Response-locked epochs were created from -600 to 1000 ms around the response, baseline corrected using the -400 to -200 ms pre-response period (Olvet & Hajcak, 2009; Pontifex et al., 2010), and filtered using a zero phase shift 1 Hz (24 dB/octave) to 12 Hz (24 dB/octave) band-pass filter. Average ERP waveforms were created for error of commission trials and correct trials, which were individually matched (without replacement) to an error of commission trial with the closest possible RT latency (Coles, Scheffers, & Holroyd, 2001), to account for potential artifacts that may exist due to differences in response latency between correct and incorrect trials (Falkenstein et al., 2001; Mathewson, Dywan, & Segalowitz, 2005). Trials with an error of omission or artifact exceeding ±75 µV were rejected. The ERN

component was evaluated as the mean amplitude within a 50 ms interval surrounding the largest negative going peak within a 0 – 150 ms window relative to the response.

Academic Achievement Assessment

Participants completed the Wide Range Achievement Test - 3rd edition (WRAT3; Wide Range, Inc., Wilmington, DE) to assess aptitude in reading, spelling, and arithmetic. The WRAT3 allows for repeated administration through the use of two equivalent forms designed specifically for pre- and post- intervention testing (Wilkinson, 1993). The WRAT3 is strongly correlated with the California Achievement Test – Form E and the Stanford Achievement Test (Wilkinson, 1993). Administration of the WRAT3 was conducted by trained experimenters with the order of the subtests presented in a counterbalanced order with the duration of the assessment taking approximately 15 minutes.

Cardiorespiratory Fitness Assessment

Maximal oxygen consumption (VO$_2$max) was measured using a computerized indirect calorimetry system (ParvoMedics True Max 2400) with averages for oxygen uptake (VO$_2$) and respiratory exchange ratio (RER) assessed every 20 seconds. A modified Balke protocol (ACSM, 2006) was employed using a motor-driven treadmill at a constant speed with increases in grade increments of 2.5% every two minutes until volitional exhaustion occurred. A Polar heart rate monitor (Polar WearLink®+ 31, Polar Electro, Finland) was used to measure HR throughout the test and ratings of perceived exertion (RPE) were assessed every two minutes using the children's OMNI scale (Utter, Roberson, Nieman, & Kang, 2002). The children's OMNI scale for RPE uses a numerical scale from 0 to 10, with a score of 2 indicating "a little tired" and a score of 9 indicating "very, very tired", with associated pictographs representing perceived physical effort. Relative peak oxygen consumption was expressed in ml/kg/min and was based

upon maximal effort as evidenced by: 1) a plateau in oxygen consumption corresponding to an increase of less than 2 ml/kg/min despite an increase in workload, 2) a peak heart rate > 185 bpm (ACSM, 2006) and a heart rate plateau (Freedson & Goodman, 1993); 3) RER > 1.0 (Bar-Or, 1983); and/or 4) ratings on the children's OMNI scale of perceived exertion > 8 (Utter et al., 2002).

Procedure

A within-participants design had participants visit the laboratory on three separate days in which they had not previously participated in physical education or other structured physical activities. During the first visit, participants and their legal guardians were provided a detailed explanation of the purpose of the research and its potential risks and were given the opportunity to ask questions prior to obtaining informed written assent from the participant and consent from their legal guardian. Following completion of the informed consent/assent, participants completed the Edinburgh Handedness Inventory (Oldfield, 1971), the K-BIT (Kaufman & Kaufman, 1990), and a VO$_2$max test. Concurrently, participants' legal guardians completed the Physical Activity Readiness Questionnaire (Thomas et al., 1992), the modified Tanner Staging System questionnaire (Taylor et al., 2001), the Social Communication Questionnaire (Rutter et al., 2003), the Child Behavioral Checklist (Achenbach & Rescorla, 2001), the ADHD Rating Scale IV (DuPaul et al., 1998), the Disruptive Behavior Rating Scale (Erford, 1993), and a health history and demographics questionnaire.

Participants were then counterbalanced into two different session orders such that half of the participants received the resting session on the second day and the aerobic exercise session on the third day. The other half received the aerobic exercise session on the second day and the resting session on the third day. During each visit, heart rate (HR) was measured at 2 minute

intervals throughout the entire session using a Polar heart rate monitor (Polar WearLink®+ 31, Polar Electro, Finland). The experimental conditions consisted of 20 minutes of either seated reading or aerobic exercise on a motor-driven treadmill at an intensity between 65% and 75% of their maximum heart rate (M = 70.2 ± 0.8% HRmax). Following the completion of the experimental conditions, participants were outfitted with an electrode cap and provided task instructions and forty practice trials. Once HR returned to within 10% of pre-experimental condition levels, the two conditions of the modified flanker task were preformed (Compatible: 16.0 ± 0.6 minutes post exercise; Incompatible: 27.4 ± 0.8 minutes post exercise) followed by administration of the WRAT3 (38.1 ± 1.4 minutes post exercise). Upon completion of the study, participants and their legal guardians were briefed on the purpose of the experiment and received $40 remuneration ($10/hour) for their involvement in the experiment.

Statistical Analysis

All statistical analyses were conducted using a significance level of $p = .05$, and analyses with three or more within-subjects levels used the Greenhouse-Geisser statistic with subsidiary univariate ANOVAs and Bonferroni corrected t tests for post hoc comparisons. The family-wise alpha level was set at 0.05. Prior to hypothesis testing, preliminary analysis were conducted to ensure that the ADHD and healthy match-control group did not significantly differ on any factors known to influence cognitive function in this age group (e.g., SES, age, pubertal timing, sex, etc.). Additionally, analysis were conducted to examine the order in which the sessions occurred to ensure that the observed effects were not due to the specific order in which participants received the exercise and rest conditions. These analyses employed an additional between-subjects variable with two levels (Session Order: Post Reading, Post Exercise vs. Post Exercise, Post Reading) to the analyses described below for each dependent measure.

Analysis of task performance measures (median RT and response accuracy) was conducted separately using a 2 (Group: ADHD, Healthy Match-Control) × 2 (Session: Post Exercise, Post Reading) × 2 (Compatibility: Compatible, Incompatible) × 2 (Congruency: Congruent, Incongruent) multivariate repeated measures ANOVA. Secondary analyses examined task performance interference scores using a 2 (Group: ADHD, Healthy Match-Control) × 2 (Session: Post Exercise, Post Reading) × 2 (Compatibility: Compatible, Incompatible) multivariate repeated measures ANOVA. Post trial task performance was also assessed using a 2 (Group: ADHD, Healthy Match-Control) × 2 (Session: Post Exercise, Post Reading) × 2 (Compatibility: Compatible, Incompatible) × 2 (Accuracy: Post Error, Post Match Correct) multivariate repeated measures ANOVA.

The N2 and P3 ERP components were assessed separately for amplitude and latency using a 2 (Group: ADHD, Healthy Match-Control) × 2 (Session: Post Exercise, Post Reading) × 2 (Compatibility: Compatible, Incompatible) × 2 (Congruency: Congruent, Incongruent) × 7 (Site: Fz, FCz, Cz, CPz, Pz, POz, Oz) multivariate repeated measures ANOVA. The ERN component was assessed at the FCz electrode site (Carter et al., 1998; Dehaene et al., 1994; Miltner et al., 2003) using a 2 (Group: ADHD, Healthy Match-Control) × 2 (Session: Post Exercise, Post Reading) × 2 (Accuracy: Error, Match Correct) multivariate repeated measures ANOVA.

Finally, analysis of academic achievement was conducted separately for each academic achievement subject (reading comprehension, spelling, arithmetic) using a 2 (Group: ADHD, Healthy Match-Control) × 2 (Session: Post Exercise, Post Reading) repeated measures ANOVA.

Tables

Table 3.1.

Inclusion Criteria for Participant Acceptance into the Current Project

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Inclusion Criteria for All Participants

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1. 8–10 years of age

2. Physically capable of performing exercise based on the PAR-Q and the Health History & Demographics Questionnaire.

3. Normal or corrected-to-normal vision

4. Free of any central nervous system-active pharmacologic therapy for at least 1 month prior to testing. However, no participant was taken off medication specifically for this investigation.

5. Pubertal status at or below 2 on the Tanner Staging System questionnaire.

6. Free of autistic spectrum disorders with scores below 15 on the Social Communication Questionnaire.

7. Free of affective disorders (including depressive and bipolar disorders), anxiety disorders, conduct disorders, and somatic disorders using the Child Behavioral Checklist with DSM-oriented scores falling below the 93rd percentile.

8. K-BIT composite score at or above 85.

Inclusion Criteria for ADHD participants	Inclusion Criteria Healthy-Control participants
1. Verified clinical status using the ADHD supplement of the K-SADS semi-structured diagnostic interview using DSM-IV-TR criteria for any subtype of ADHD, including evidence for impairment in two or more settings and onset of symptoms before 7 years of age. 2. Ongoing ADHD symptoms as indicated by a score at or above the 90th percentile on the ADHD Rating Scale-IV.	1. Free of ADHD disorders as measured by a: a. Score below the 80th percentile on the ADHD Rating Scale IV – Parent Version b. T-score below 60 on the Disruptive Behavior Rating Scale – Parent Version c. Score below the 93rd percentile on the DSM-oriented scale of Attention Deficit /Hyperactivity problems of the Child Behavioral Checklist.

Figures

Figure 3.1. Illustration of the congruent (A) and incongruent (B) fish stimuli used in the modified

flanker task.
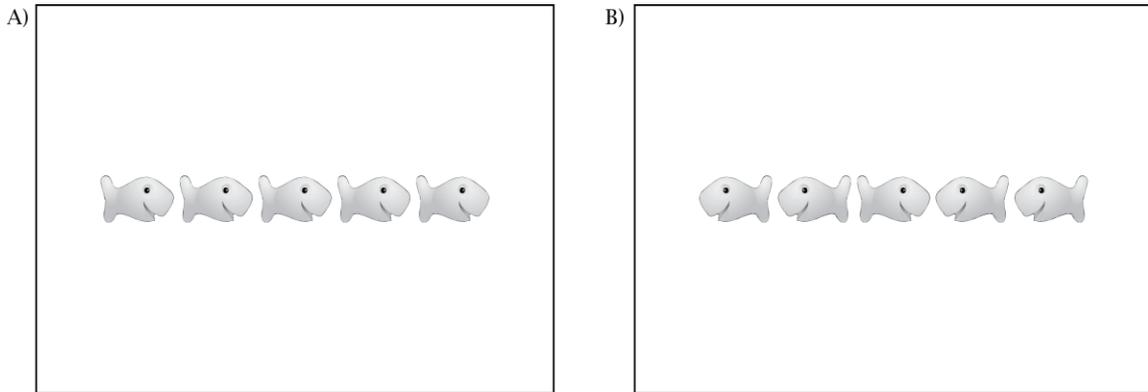
Chapter 4

Results

The results section is organized according to dependent measure. First, participant characteristics are reported in relation to ADHD status. Second, task performance measures of median reaction time, response accuracy, interference scores, and post trial performance are reviewed. Next, analyses of the neuroelectric components are provided (N2, P3, and ERN) with amplitude presented first followed by latency within each component. Finally, academic achievement findings are reviewed.

Participant Characteristics

Participant demographics and clinical characteristics are provided in Table 4.1. No significant differences between groups were observed for Age, Pubertal Timing, IQ, or SES, $t's$ (38) $\leq$ 1.6, $p's \geq 0.116$, confirming the efficacy of the participant matching procedure. Clinical characteristics of the ADHD group, split based upon ADHD subtype using the K-SADS diagnostic interview classification, are provided in Table 4.2. No significant differences in HR were observed between ADHD and healthy match-control groups for any condition, $t's$ (38) $\leq$ 1.3, $p's \geq 0.207$ (see Figure 4.1).

Preliminary analyses were performed to test whether Session Order, which was counterbalanced across participants, was related to any of the dependent variables. Findings revealed no significant main effects or interactions involving Session Order for any variable, $F's$ (1,38) $\leq$ 3.2, $p \geq 0.08$, $\eta_p^2 \leq 0.08$. Thus, all further analyses were collapsed across Session Order.

Task Performance

      Reaction time.

Analysis revealed main effects of Compatibility, with longer RT latency for the incompatible (509.0 ± 17.2 ms) relative to the compatible (493.0 ± 17.4 ms) condition, F (1,38) $= 6.9$, $p = 0.01$, $\eta_p^2 = 0.15$; and Congruency, with longer RT latency for incongruent (515.6 ± 17.1 ms) relative to congruent (486.5 ± 17.0 ms) trials, F (1,38) $= 198.3$, $p < 0.001$, $\eta_p^2 = 0.84$. No main effects or interactions involving Group or Session were observed for RT latency, $F's$ (1,38) ≤ 2.8, $p \geq 0.1$, $\eta_p^2 \leq 0.07$ (see Figure 4.2).

Response accuracy.

Analysis revealed main effects of Group, with decreased response accuracy for the ADHD (81.8 ± 2.7 %) relative to the control (88.8 ± 1.3 %) group, F (1,38) $= 5.4$, $p = 0.026$, $\eta_p^2 = 0.12$; and Session, with increased response accuracy post exercise (87.1 ± 1.7 %) relative to post reading (83.5 ± 1.8 %), F (1,38) $= 7.1$, $p = 0.011$, $\eta_p^2 = 0.16$ (see Figure 4.2). Further, main effects of Compatibility, F (1,38) $= 16.1$, $p < 0.001$, $\eta_p^2 = 0.3$; and Congruency, F (1,38) $= 58.8$, $p < 0.001$, $\eta_p^2 = 0.6$, were observed with increased response accuracy for compatible (86.7 ± 1.5 %) and congruent (87.8 ± 1.4 %) trials relative to incompatible (83.8 ± 1.7 %) and incongruent (82.7 ± 1.7 %) trials.

Interference score.

No significant findings were observed for median RT latency or response accuracy interference scores, $F's$ (1,38) ≤ 3.4, $p \geq 0.07$, $\eta_p^2 \leq 0.08$.

Post trial performance.

Analysis of post-trial latency revealed a main effect of Accuracy, F (1,38) $= 20.3$, $p < 0.001$, $\eta_p^2 = 0.35$, which was superseded by an interaction of Group $\times$ Session $\times$ Accuracy, F (1,38) $= 6.2$, $p = 0.017$, $\eta_p^2 = 0.14$. Decomposition of the Group $\times$ Session $\times$ Accuracy interaction occurred by assessing Group $\times$ Session within each accuracy condition and revealed

greater post-error slowing following the exercise condition (579.4 ± 35.1 ms) relative to following the reading condition (500.3 ± 32.4 ms) only for the ADHD group, t (19) = 3.0, $p = 0.008$, see Figure 4.3. A main effect of Compatibility, F (1,38) = 13.8, $p = 0.001$, $\eta_p^2 = 0.27$, was also observed with increased post-trial latency for incompatible (525.0 ± 18.8 ms) relative to compatible (492.3 ± 17.9 ms) trials. No main effects or interactions involving Group or Session were observed for post-trial accuracy, $F's$ (1,38) ≤ 3.0, $p \geq 0.09$, $\eta_p^2 \leq 0.07$.

Event-related Brain Potentials

Preliminary analyses were conducted on the number of trials included in both stimulus-locked ERP averages and response-locked ERP averages to ensure that any observed effects were not the result of different numbers of included trials. Analyses of the number of trials included in stimulus-locked averages revealed no significant differences for any of the dependent variables of interest, $F's$ (1,38) ≤ 2.4, $p \geq 0.13$, $\eta_p^2 \leq 0.06$. Analysis conducted on the number of error/correct trials included in response-locked ERP averages similarly revealed no significant differences for any of the dependent variables of interest, $F's$ (1,34) ≤ 3.6, $p \geq 0.07$, $\eta_p^2 \leq 0.09$.

N2.

Amplitude.

Figure 4.4 illustrates the grand average stimulus-locked ERP waveforms for each group and session. Analysis of N2 amplitude revealed main effects of Session, F (1,38) = 12.5, $p = 0.001$, $\eta_p^2 = 0.25$; and Site, F (6,38) = 15.2, $p < 0.001$, $\eta_p^2 = 0.29$; which were superseded by an interaction of Session $\times$ Site, F (6,38) = 4.8, $p = 0.008$, $\eta_p^2 = 0.11$. Decomposition of the interaction of Session $\times$ Site revealed reduced N2 amplitude following exercise relative to following reading at the Fz, FCz, Cz, and CPz electrode sites, $t's$ (39) ≥ 3.5, $p \leq 0.001$. A main

effect of Compatibility, F (1,38) = 13.0, p = 0.001, η_p^2 = 0.25, was also observed with larger N2 amplitude for compatible (-3.2 ± 0.7 μV) relative to incompatible (-1.6 ± 0.6 μV) trials.

Latency.

Analysis of N2 latency revealed a main effect of Session, F (1,38) = 12.1, p = 0.001, η_p^2 = 0.24, which was superseded by an interaction of Group × Session × Congruency, F (1,38) = 8.2, p = 0.007, η_p^2 = 0.18. Decomposition of the Group × Session × Congruency interaction was conducted by assessing Group × Session within each congruency condition (see Figure 4.5). Analysis of Group × Session within congruent trials revealed a main effect of Session, F (1,38) = 8.6, p = 0.006, η_p^2 = 0.19, which was superseded by a Group × Session interaction, F (1,38) = 4.1, p = 0.049, η_p^2 = 0.1. Decomposition of the Group × Session interaction within congruent trials revealed longer N2 latency for the ADHD group (273.7 ± 8.9 ms) relative to the Healthy Match-Control group (249.0 ± 5.3 ms) only following reading, t (38) = 2.4, p = 0.023. No group differences in N2 latency were observed following exercise (ADHD: 248.2 ± 8.1 ms; Healthy Match-Control: 244.3 ± 5.7 ms), t (38) = 0.4, p = 0.7. Analysis of Group × Session within incongruent trials only revealed a main effect of Session, F (1,38) = 12.5, p = 0.001, η_p^2 = 0.25, with shorter N2 latency following exercise (245.4 ± 5.2 ms) relative to following reading (264.1 ± 5.4 ms). A main effect of Site, F (6,38) = 7.0, p = 0.001, η_p^2 = 0.16, was also observed with shorter N2 latency for the Cz and CPz electrode sites relative to the Fz and FCz electrode sites, t's (39) ≥ 4.4, p ≤ 0.001.

P3.

Amplitude.

Figure 4.4 illustrates the grand average stimulus-locked ERP waveforms for each group and session. Analysis of P3 amplitude revealed main effects of Session, F (1,38) = 25.9, p <

0.001, $\eta_p^2 = 0.41$, with increased P3 amplitude following exercise (10.9 ± 0.6 µV) relative to

following reading (7.9 ± 0.5 µV); and Site, F (6,38) = 7.8, $p < 0.001$, $\eta_p^2 = 0.17$, with smaller P3

amplitude at Fz relative to all other electrode sites, $t's$ (39) ≥ 3.7, p ≤ .001. A main effect of

Group was also observed, F (1,38) = 4.3, $p = 0.044$, $\eta_p^2 = 0.1$; which was superseded by an

interaction of Group × Congruency, F (1,38) = 5.9, $p = 0.02$, $\eta_p^2 = 0.14$. Decomposition of the

Group × Congruency interaction revealed smaller P3 amplitude for the ADHD group (7.8 ± 0.6

µV) relative to the Healthy Match-Control group (10.1 ± 0.6 µV), only for incongruent trials, t

(38) = 2.8, $p = 0.009$.

Latency.

Analysis of P3 latency revealed main effects of Session, F (1,38) = 13.0, $p = 0.001$, $\eta_p^2 =$

0.25; and Site, F (6,38) = 12.5, $p < 0.001$, $\eta_p^2 = 0.25$; which were superseded by an interaction of

Session × Site, F (6,38) = 3.1, $p = 0.025$, $\eta_p^2 = 0.08$. Decomposition of the Session × Site

interaction revealed shorter P3 latency following exercise relative to following reading only at

the FCz, Cz, and CPz electrode sites, $t's$ (39) ≥ 3.1, $p ≤ 0.004$ (see Figure 4.6). Main effects of

Compatibility, F (1,38) = 9.2, $p = 0.004$, $\eta_p^2 = 0.2$; and Congruency, F (1,38) = 14.8, $p < 0.001$,

$\eta_p^2 = 0.28$, were also observed with shorter P3 latency for compatible (401.7 ± 8.2 ms) and

congruent (401.6 ± 7.8 ms) trials relative to incompatible (417.9 ± 7.8 ms) and incongruent

(418.0 ± 7.9 ms) trials.

ERN.

Previous research has established that a minimum of six error of commission trials are

necessary to obtain a stable ERN component (Olvet & Hajcak, 2009; Pontifex et al., 2010).

Accordingly, an insufficient number of participants (N = 12 ADHD, 11 Healthy Match-Control)

exhibited the necessary number of trials within each compatibility condition to parse the separate

effects of Group and Session on ERN amplitude within each compatibility condition.

Accordingly, compatible and incompatible trials were collapsed after matching error and correct trials within each compatibility. Remaining participants with fewer than six errors of commission were discarded from analysis of the ERN component (N = 4; 2 ADHD), leaving a total of 36 participants. No significant differences between Groups were observed in this subset of participants for Age, Pubertal Timing, IQ, or SES, t's (34) $\leq$ 1.8, p's $\geq$ 0.089.

Analysis of ERN amplitude revealed a main effect of Accuracy, F (1,34) = 115.9, $p <$ 0.001, η_p^2 = 0.77, which was superseded by interactions of Session $\times$ Accuracy, F (1,34) = 7.5, p = 0.01, η_p^2 = 0.18, and Group $\times$ Session $\times$ Accuracy, F (1,34) = 5.4, p = 0.026, η_p^2 = 0.14. Decomposition of the Group $\times$ Session $\times$ Accuracy interaction was conducted by assessing Group $\times$ Session within each accuracy condition. Analysis of Group $\times$ Session within error trials revealed an interaction of Group $\times$ Session, F (1,34) = 4.1, p = 0.05, η_p^2 = 0.11, with smaller ERN amplitude for the ADHD group (-7.3 $\pm$ 1.1 μV) relative to the Healthy Match-Control group (-11.2 $\pm$ 1.1 μV) only following the reading session, t (34) = 2.5, p = 0.017 (see Figure 4.7). No group differences were observed following exercise, t (34) = 0.03, p = 0.98. Similarly, analysis of Group $\times$ Session within match-correct trials revealed no main effects or interactions involving Group or Session, F's (1,34) $\leq$ 1.6, $p \geq$ 0.21, $\eta_p^2 \leq$ 0.05.

Academic Achievement

Analysis of the three subtest of the WRAT3 revealed main effects of Session for reading comprehension, F (1,38) = 20.1, $p <$ 0.001, η_p^2 = 0.35; and arithmetic, F (1,38) = 5.0, p = 0.032, η_p^2 = 0.12; with increased performance following exercise (reading comprehension: 115.2 $\pm$ 2.2; arithmetic: 112.5 $\pm$ 2.7) relative to following reading (reading comprehension: 110.1 $\pm$ 1.8;

arithmetic: 110.0 ± 3.1). No main effects or interactions involving Group or Session were observed for spelling, $F's$ $(1,38) \leq 2.2$, $p \geq 0.15$, $\eta_p^2 \leq 0.05$ (see Figure 4.8).

Tables

Table 4.1.

Participant demographic values (± 1 SE).

Measure	ADHD	Healthy Match-Control
N	20 (6 females)	20 (6 females)
Age (years)	9.5 ± 0.2	9.8 ± 0.14
Tanner stage	1.4 ± 0.1	1.4 ± 0.1
K-BIT composite (IQ)	112.3 ± 2.7	118.7 ± 2.9
Socioeconomic status (SES)	2.3 ± 0.2	2.3 ± 0.2
ADHD rating scale-IV (composite)	$97.0 \pm 1.1^{\dagger}$	$31.3 \pm 4.2^{\dagger}$
Disruptive behavior rating scale (composite ADHD)	$61.9 \pm 2.5^{\dagger}$	$44.8 \pm 1.0^{\dagger}$
Oppositional defiance disorder score	$52.3 \pm 2.2^{\dagger}$	$43.7 \pm 1.0^{\dagger}$
Autism spectrum disorder score	5.7 ± 0.7	3.5 ± 0.8
Body mass index (kg/m^2)	17.3 ± 0.6	20.0 ± 1.2
VO$_2$max (ml/kg/min)	43.0 ± 1.1	40.5 ± 1.1
HRmax (bpm)	187.9 ± 2.7	190.2 ± 2.9

Note: ADHD rating scale-IV – percentile for the composite subscale of the ADHD-IV rating scale. Disruptive behavior rating scale – T-score from the DBRS distractible and impulsive-hyperactive subscales. Oppositional defiance disorder score – T-score from the DBRS oppositional defiance disorder subscale. Autism spectrum disorder score – total score on the Social Communication Questionnaire. [†] $p \leq 0.001$.

Table 4.2.

Clinical characteristics of the ADHD group (±1 SE).

Measure	ADHD Subtype		
	ADHD-C	ADHD-I	ADHD-H
N	6 (2 females)	11 (3 females)	3 (1 female)
K-SADS inattentive symptoms	7.3 ± 0.3	7.0 ± 0.3	3.7 ± 1.3
K-SADS impulsive/hyperactive symptoms	6.5 ± 0.2	3.3 ± 0.4	8.0 ± 1.0
ADHD-IV composite percentile	98.2 ± 1.3	98.2 ± 0.7	90.0 ± 5.5
ADHD-IV inattentive percentile	92.7 ± 4.1	92.0 ± 2.2	62.3 ± 12.3
ADHD-IV impulsive/hyperactive percentile	94.5 ± 2.1	80.5 ± 6.1	91.3 ± 0.9
DBRS distractible subscale T-score	66.2 ± 6.5	64.7 ± 3.5	49.3 ± 2.9
DBRS impulsive-hyperactive subscale T-score	65.5 ± 4.5	59.8 ± 3.2	56.0 ± 6.4
DBRS oppositional defiance disorder subscale T-score	57.0 ± 3.5	51.0 ± 3.3	47.7 ± 4.3
Autism spectrum disorder score	7.0 ± 1.1	4.6 ± 1.0	7.3 ± 0.9

Note: ADHD subtype was based upon K-SADS diagnostic interview classification. Percentiles greater than or equal to 90 on the ADHD-IV rating scale indicate high likelihood for the presence of ADHD. T-scores below 60 on the DBRS are considered to be normal behavioral ratings. Autism spectrum disorder scores below 15 indicate the absence of autism spectrum disorders.

**Figures**
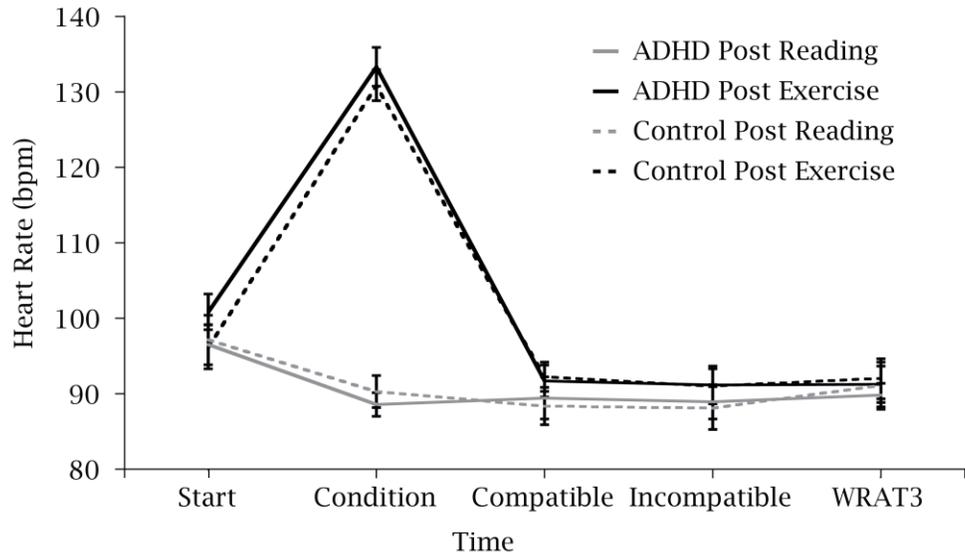
Figure 4.1. Mean HR (± SE) over the course of each of the experimental sessions by group.
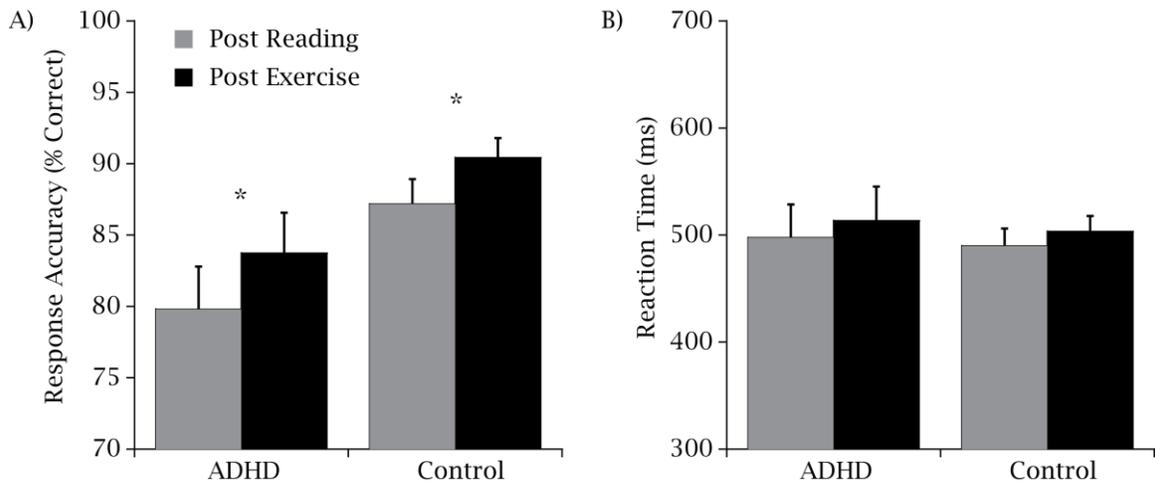
Figure 4.2. Mean (± SE) response accuracy (A) and median (± SE) reaction time (B) for each

session by group collapsed across compatibility and congruency conditions.
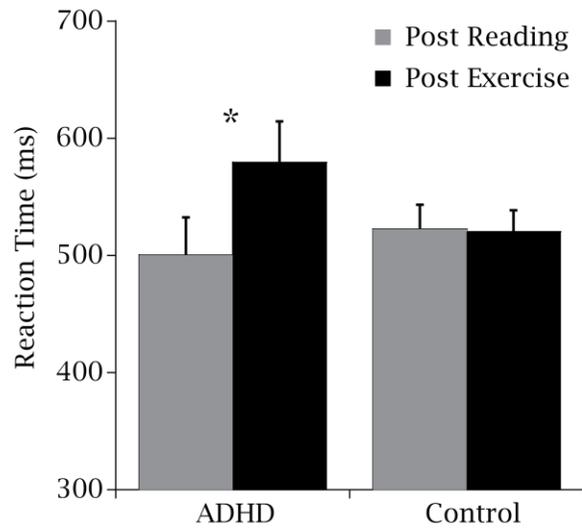
Figure 4.3. Mean (± SE) post error latency for each session by group collapsed across

compatibility and congruency conditions.
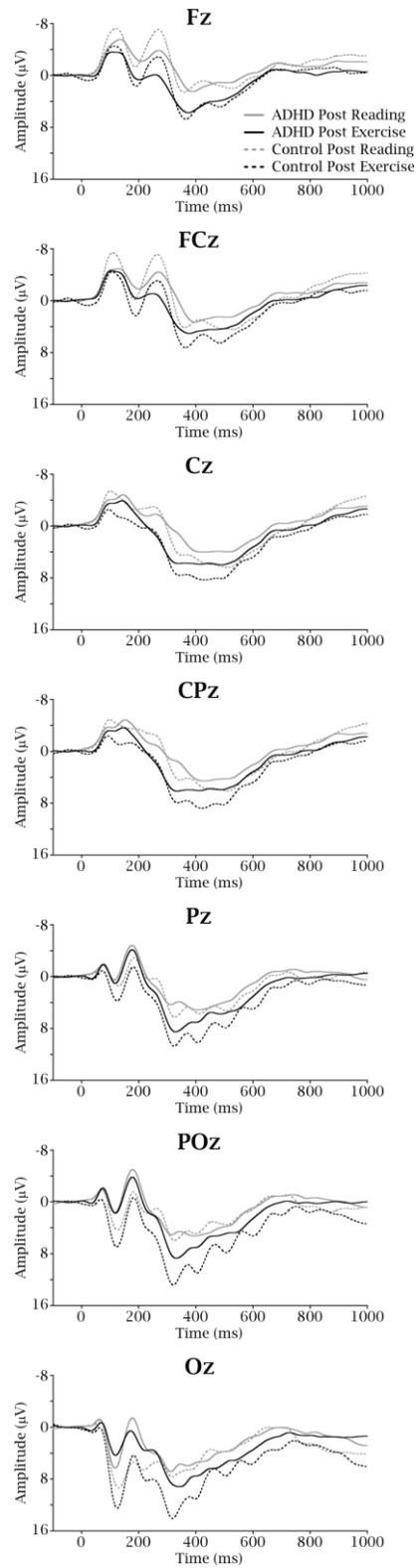
Figure 4.4. Stimulus-locked grand-average waveforms for each group and session collapsed

across compatibility and congruency conditions.
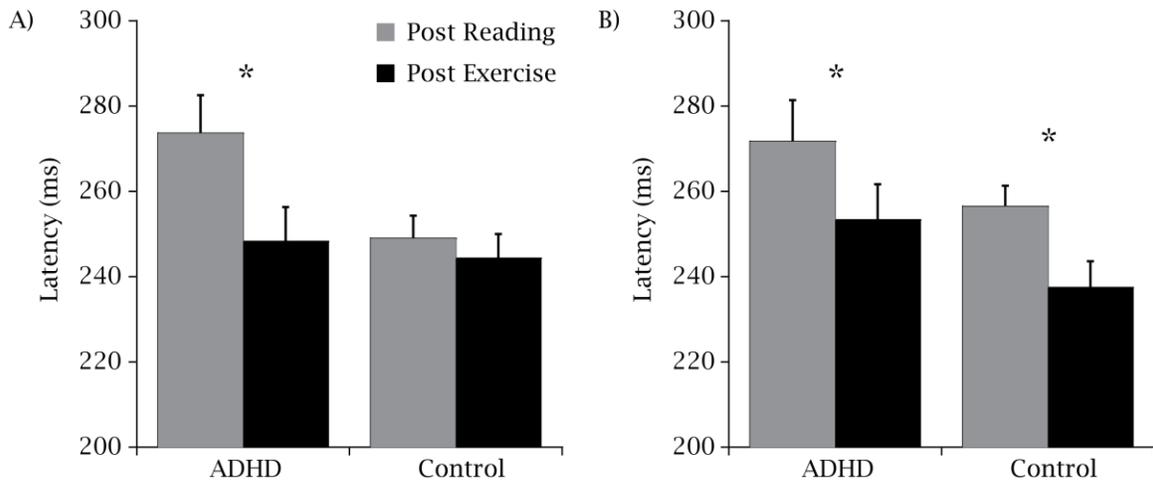
Figure 4.5. Mean (± SE) N2 latency for each session by group for congruent (A) and incongruent (B) trials collapsed across compatibility conditions.
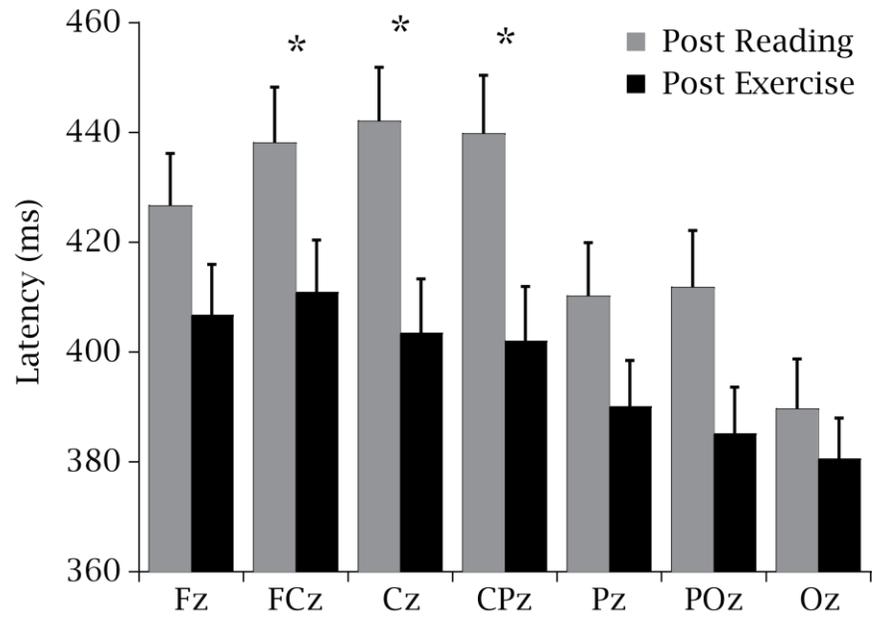
Figure 4.6. Mean (± SE) P3 latency for each session by midline electrode site collapsed across

group and the compatibility and congruency conditions..
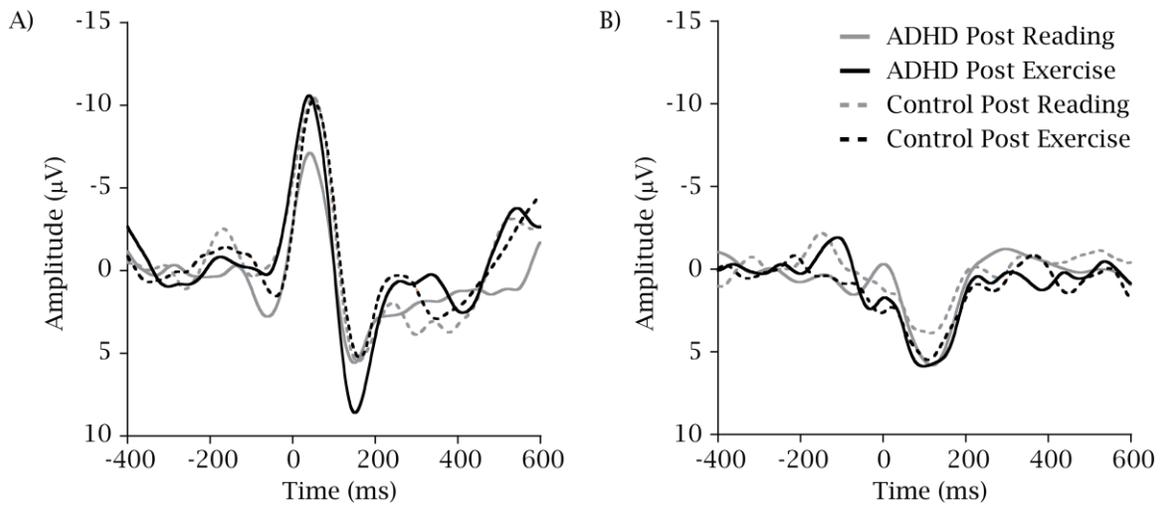
Figure 4.7. Response-locked grand-average waveforms for error (A) and match-correct (B)

trials.
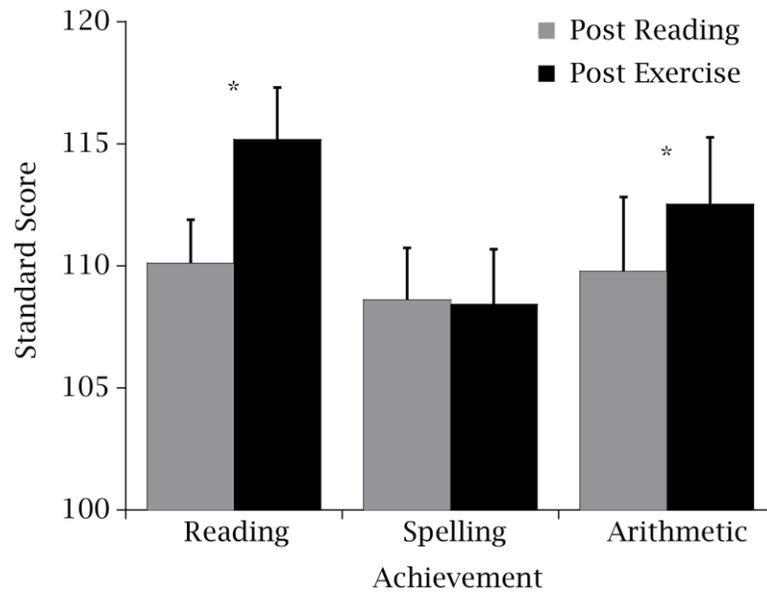
Figure 4.8. Mean (± SE) standard score for each session on each of the three WRAT3 achievement tests.

Chapter 5
Discussion

In this investigation, the extent to which a single bout of moderate-intensity aerobic physical activity might be effective in transiently improving behavioral and neuroelectric deficits in cognition associated with ADHD was assessed. Findings revealed that acute exercise served to enhance neuroelectric and behavioral indices of performance in children with ADHD and healthy controls. Specifically, following 20 minutes of aerobic exercise, both children with ADHD and healthy match-control children exhibited greater overall response accuracy across compatibility conditions of the modified flanker task; relative to following a similar duration of seated rest in which they were afforded the opportunity to read literature of their choosing. Neuroelectric findings revealed decreased N2 amplitude, increased P3 amplitude, and shorter N2 and P3 latency following exercise, relative to following reading; suggesting that a single bout of exercise served to reduce response conflict and enhance the allocation of attentional resources, response selection processes, and stimulus classification/processing speed. Further, children with ADHD exhibited additional exercise induced enhancements in cognition, with facilitations in action monitoring processes and greater post-error slowing following exercise, relative to following reading. Scholastic benefits were also observed following exercise, in that both children with ADHD and healthy match-control children exhibiting improved performance on academic achievement tests of reading comprehension and arithmetic. Thus, these data indicate that acute exercise might serve as a transient, cost-effective means for improving the cognitive health, academic performance, and overall effective functioning of both "normal" prototypical preadolescent children and children with ADHD.

Task Performance

Replicating previous investigations, deficits in inhibitory control were observed for children with ADHD, with decreased overall response accuracy relative to healthy match-control children (Albrecht et al., 2008; Booth et al., 2007; Crone et al., 2003; Jonkman et al., 1999; Konrad et al., 2006; Scheres et al., 2004; Vaidya et al., 2005; van Meel et al., 2007). Further, the size of this observed deficit (Cohen's $d = 0.74$) is consistent with the extant literature, as meta-analyses have indicated moderate effect sizes ranging from 0.69 to 0.75 for ADHD-related deficits in inhibitory control (Homack & Riccio, 2004; Pennington & Ozonoff, 1996). Novel to this investigation, however, was the inclusion of the stimulus-response manipulation during the flanker task. Replicating the findings of Friedman et al. (2009) and Pontifex et al. (2011), decreased response accuracy was observed for the incompatible stimulus-response mapping relative to the compatible stimulus-response mapping, suggesting that the stimulus-response manipulation engendered greater inhibitory control requirements. Despite the fact that the interaction of Group and Compatibility did not reach a level of statistical significance ($p = 0.08$), examination of the absolute means for response accuracy suggests that inhibitory deficits associated with ADHD were larger for the incompatible condition (Cohen's $d = 0.79$) relative to the compatible condition (Cohen's $d = 0.63$). In line with previous assertions, this trend suggests that ADHD related deficits in performance are magnified with greater inhibitory control demands.

Germane to the focus of this investigation, however, was the extent to which a single bout of moderately intense aerobic exercise might be effective in reducing these ADHD-related deficits in inhibitory control. Although findings from this investigation revealed that children with ADHD did not experience a disproportionately greater exercise induced enhancement in response accuracy relative to healthy match-control children, a single bout of exercise did serve

to enhance the overall response accuracy of children with ADHD by almost 5% (Cohen's d = 0.3), relative to following reading. Accordingly, findings from this investigation revealed that both children with ADHD, and healthy-match control children, exhibited similar overall enhancements in behavioral indices of inhibitory control following a single 20 minute bout of exercise. Thus, these findings add to a growing body of research demonstrating that a single, short duration bout of aerobic exercise is beneficial for inhibitory aspects of cognitive control (Hillman, Pontifex et al., 2009; Hogervorst et al., 1996; Kamijo et al., 2007; Lichtman & Poser, 1983; Sibley et al., 2006; Tomporowski et al., 2005), and suggest that short bouts of aerobic physical activity may be equally beneficial for healthy children and children with attentional disorders. It is important to note, however, that replicating previous findings (Hillman, Pontifex et al., 2009) these exercise-induced enhancements in response accuracy were observed in the absence of modulations in the speed of children's responses. The absence of such an effect was not unexpected however, as previous research has observed that preadolescent children, particularly those with ADHD, exhibit greater impulsivity in responding than adults with less modulation of their RT (Albrecht et al., 2008; Booth et al., 2007; Crone et al., 2003; Davidson et al., 2006; Jonkman et al., 1999). Thus, although median RT was used within the present investigation to better represent intra-individual trends in RT, and findings do replicate previous investigations observing robust differences in RT between congruency (Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002; Hillman, Pontifex et al., 2009; Mezzacappa, 2004; Pontifex et al., 2011) and compatibility (Pontifex et al., 2011) conditions, no group or session differences were observed for RT latency.

Interestingly, although exercise induced enhancements in response accuracy were observed for both children with ADHD and healthy control children; a selective enhancement in

post-error slowing was observed only for children with ADHD following exercise relative to following reading. Post-error slowing is believed to serve as a behavioral indicator of the increased recruitment and implementation of top-down attentional control in order to improve subsequent interactions within the environment (Gehring et al., 1993; Kerns et al., 2004). Therefore, these findings suggest that following a single bout of exercise, relative to following a similar duration of reading, children with ADHD may be better capable of regulatory adjustments in behavior following the commission of an error thus enhancing future performance. Further, these findings replicate previous research in children (Hillman, Pontifex et al., 2009) and young adults (Hillman et al., 2003; Kamijo et al., 2007, 2009), which have failed to observe exercise-induced modulations in post-error slowing in healthy populations. Thus, it may be that healthy individuals already operate at a relative peak regulatory capacity, and as such, do not derive regulatory benefits from single bouts of physical activity; while the compromised nature of inhibitory control in children with ADHD may allow for these exercise-induced enhancements in regulatory adjustments in behavior to be observed.

Event-Related Brain Potentials

A more precise understanding of the relationship between acute exercise and ADHD may be provided through the assessment of the specific component processes that underlie goal-direction behavior. One neuroelectric potential, which has been extensively studied and been found sensitive to both ADHD-related deficits, and exercise-induced enhancements, is the P3 ERP. With regard to the relationship between ADHD and P3 amplitude, findings from the present investigation revealed smaller P3 amplitude for children with ADHD, relative to healthy match-control children, only in response to the incongruent trials replicating previous research that has observed ADHD-related deficits in the allocation of attentional resources for task

conditions requiring the greatest amount of inhibitory control (Jonkman et al., 1999). Novel to the present investigation, however, was the assessment of exercise-induced modulations in P3 amplitude in children with ADHD. Findings revealed that following a single bout of exercise, a general enhancement in P3 amplitude was observed for both children with ADHD and healthy-match control children, relative to reading. Interestingly, the findings in healthy children reported herein do not perfectly replicate those observed by Hillman, Pontifex, and colleagues (2009) who observed selective enhancements in response accuracy and P3 amplitude only for incongruent trials of the flanker task following a single bout of similar duration exercise in a sample of healthy preadolescent children. However, it is important to note that the effect of acute exercise on congruent trials was marginally significant in that investigation (Hillman, Pontifex et al., 2009). Thus, a number of factors, both methodological and statistical, may be responsible for the general effects observed within the present investigation. That is, given the absence of Group by Session interactions for response accuracy and P3 amplitude, these analyses benefitted from an increase in statistical power provided by the additional 20 children with ADHD, which may have allowed the effect of exercise on congruent trials to reach statistical significance. Another possibility is that the greater inhibitory control requirements of the congruent stimulus-response incompatible trials may have served to enhance the overall inhibitory control necessary for congruent trials. Given that previous research has suggested that exercise exerts a selectively larger influence over task components with larger inhibitory control demands (Hogervorst et al., 1996; Kamijo et al., 2007; Lichtman & Poser, 1983; Sibley et al., 2006; Tomporowski et al., 2005), this increased inhibitory requirement for congruent trials may have resulted in a greater exercise induced enhancement. Lastly, the exercise intensity of the present investigations may also be responsible for the general effects observed within the present investigation. That is, as

has been frequently posited in the literature (Hillman, Kamijo, & Pontifex, in press; Kamijo et al., 2007, 2009; Tomporowski and Ellis, 1986), acute exercise-induced enhancements in cognition appear to exhibit a curvilinear relationship with exercise intensity, with intensities between 65 and 85% of HRmax appearing to exert the greatest benefit for inhibitory aspects of cognition (Hillman, Kamijo, & Pontifex, in press). Within the present investigation, children exercised at an intensity of approximately 70% of HRmax (HR = 132.1 ± 1.6 bpm), while Hillman, Pontifex, and colleagues (2009) had children exercise at approximately 65% of HRmax (HR = 125.4 ± 1.0 bpm). Although the functional differences in HR between these two investigations are diminutive, the greater exercise intensity utilized within the present investigation may have served to optimize the mechanism underlying these exercise-induced enhancements in inhibition. Consonant with this assertion, comparison of the effect of exercise on P3 amplitude between investigations reveals a larger effect of exercise for the present investigation, Cohen's $d = 0.89$, relative to that observed by Hillman, Pontifex and colleagues (2009), Cohen's $d = 0.79$. While each of these possibilities is discussed separately, it is important to note that they are not necessarily mutually exclusive. Thus, they each may have contributed to the observed effects. Taken together, however, findings from this investigation add to a growing body of research, which has observed acute exercise induced enhancements in the allocation of attentional resources (Hillman et al., 2003; Hillman, Pontifex et al., 2009; Kamijo et al., 2004, 2007, 2009).

Another aspect of the P3 ERP that has garnered interest in both the ADHD and acute exercise literatures is its latency. Contrary to the findings of Jonkman and colleagues (1999), no ADHD related delays in stimulus classification and processing speed – as indexed by longer P3 latency – were observed in response to the flanker task within the present investigation.

Although speculative, a number of possible explanations for this discrepancy exist. One such possibility may be that these ADHD-related deficits in P3 latency manifest in a linear fashion with greater severity of ADHD. That is, the present investigation utilized a community based sample of children with suspected or diagnosed ADHD who were free of any central nervous system-active pharmacologic therapy for at least 1 month prior to testing, in contrast to the ADHD sample utilized by Jonkman and colleagues (1999) who were currently undergoing treatment within the department of Child Psychiatry of a research hospital and refrained from medication use for only 3 days prior to testing. Consequently, the participant population utilized by Jonkman and colleagues (1999) represents a sample that was experiencing greater severity of ADHD symptoms than the population tested within the current investigation. Further research is necessary, however, to fully elucidate the extent to which the severity of ADHD symptoms and delays in P3 latency may be related. Alternatively, the discrepancy between investigations may also be a function of task parameters. That is, the flanker stimuli presented within the current investigation were presented 300 ms faster than those presented by Jonkman et al. (1999), who also utilized a cue stimulus. As a result, given that the mean P3 latency for this investigation was almost 200 ms faster than that reported by Jonkman et al., (1999), even for healthy children, the speeded nature of the current task may be responsible for the observed discrepancy in P3 latency for children with ADHD.

Nevertheless, investigation of the extent to which acute exercise served to induced modulations in P3 latency in children with ADHD revealed that following a single bout of aerobic physical activity shorter P3 latency was observed, relative to following reading, in the fronto-central, central, and central-parietal electrode sites for both children with ADHD and healthy match-control children. Accordingly, these findings corroborate previous findings in

children (Hillman, Pontifex et al., 2009) and college-age young adults (Hillman et al., 2003; Kamijo et al., 2007), and older adults (Kamijo et al., 2009), and collectively support the observation of facilitations in stimulus classification and processing speed following a single bout of short duration aerobic physical activity.

Contrary to the *a priori* hypothesis that acute exercise would not modulate conflict-related processes; findings from this investigation revealed a general, yet selective, effect of exercise on the N2 and ERN components. That is, the amplitude of the fronto-central N2, which exhibits a topographic maximum over fronto-central recording sites (Folstein & Van Petten, 2008; Patel & Azzam, 2005), is believed to reflect aspects of response inhibition (Falkenstein, Hoormann, & Hohnsbein, 1999; Schmitt et al., 2000) associated with conflict monitoring processes during correct trials with greater N2 amplitude reflecting increased conflict (Ridderinkhof et al., 2002; van Veen & Carter, 2002; Yeung et al., 2004). Following a single 20-minute bout of exercise, both children with ADHD and healthy-match control children exhibited reductions in N2 amplitude over the frontal to central-parietal electrode sites, relative to seated reading. Interestingly, the selective localization of this exercise-induced reduction in response conflict to frontal cortical areas provides some support for the validity of this finding to suggest that the reduction in N2 amplitude may not simply be a byproduct of the initial generation of the exercise-induced enhancement in P3 amplitude pulling down the N2 ERP. Rather, this finding suggests that acute exercise may serve to enhance the functional integration of information within neural circuits involved in conflict monitoring.

Although to date, no prior acute exercise investigation has observed this exercise-induced reduction in response conflict, some insight into this novel finding may be provided through the investigation of N2 latency. That is, although acute exercise, relative to reading, served to

facilitate general aspects of the response selection process – as index by shorter N2 latency (Gajewski et al., 2008) – in children with ADHD; in healthy match-control children this exercise induced facilitation was only observed in response to the incongruent trials of the flanker task. However, visual inspection of the data suggests that the selective findings observed in healthy match-control children may be a product of a ceiling effect such that in healthy children, the response selection process for congruent trials was already optimized and thus was unable to benefit from acute exercise. Consequently, it may be that these exercise-induced enhancements in conflict-related processes may only manifest when inhibitory processes are compromised – as in the case of the children with ADHD – or when inhibitory control is sufficiently taxed. Thus, although no interactions with compatibility were observed for N2 amplitude or latency, the additional layering of inhibitory control required for the stimulus-response incompatible condition may have served to sufficiently tax these inhibitory processes and allowed acute exercise to exert its beneficial effect.

Consonant with this assertion, analysis of the error-related negativity revealed a selective enhancement following a bout of aerobic exercise, relative to reading, only for the children with ADHD. That is, replicating previous research that has observed ADHD related deficits in action monitoring processes (Albrecht et al., 2008; van Meel et al., 2007); children with ADHD exhibited a smaller ERN than healthy match-control children following the reading condition. However, those ADHD related deficits in action monitoring were ameliorated following just 20 minutes of aerobic exercise. As such, these findings suggest that the compromised nature of the action monitoring system in children with ADHD may have allowed acute exercise to exert its beneficial influence over the ERN.

Collectively, the present findings contribute to a greater understanding of the relationship between single bouts of aerobic physical activity and neurocognitive function as it relates to the prototypical "healthy" preadolescent population and children with ADHD. That is, findings from the present investigation suggest that single bouts of moderately intense aerobic physical activity serve to enhance inhibitory control in both children with ADHD and healthy-match control children through reductions in response conflict, and facilitations in the response selection process, the allocation of attentional resources, and stimulus-classification and processing speed. Further, children with ADHD appear to disproportionately benefit from acute exercise with additional enhancements in action monitoring processes and regulatory adjustments in behavior. Thus, these findings add to a growing body of research demonstrating that a single short duration bout of aerobic exercise is beneficial for neuroelectric and behavioral indices of inhibitory control (Hillman et al., 2003; Hillman, Pontifex et al., 2009; Hogervorst et al., 1996; Kamijo et al., 2004, 2007, 2009; Lichtman & Poser, 1983; Sibley et al., 2006; Tomporowski et al., 2005).

Academic Achievement Performance

Interesting, these exercise-induced enhancements in inhibitory aspects of cognitive control may have particular relevance for maximizing scholastic performance. That is, inhibition has been linked as a necessary faculty involved in academic achievement (Bull, Espy, & Wiebe, 2008; St. Clair-Thompson & Gathercole, 2006), with scholastic performance in the areas of reading and mathematics having been found to be heavily dependent upon the successful inhibition of unrelated information (Bull & Scerif, 2001; St. Clair-Thompson & Gathercole, 2006). Accordingly, given that acute exercise appears to enhance inhibitory control, it may also be effective in transiently reducing ADHD related deficits in scholastic achievement (Frazier, Youngstrom, Gluttig, & Watkins, 2007). While no group differences in performance were

observed for any of the subtests of the WRAT3 within the present investigation, findings did reveal that following a single bout of aerobic exercise, both children with ADHD and healthy match-control children, exhibited enhanced performance on tests of reading comprehension and arithmetic, relative to following a similar duration of reading. These findings partially replicate those of Hillman, Pontifex, and colleagues (2009) who observed acute exercise-induced enhancements in reading comprehension in a sample of healthy children. As discussed previously, it may be that the greater exercise intensity utilized within the present investigation, relative to that utilized by Hillman, Pontifex, and colleagues (2009), was necessary to engender acute exercise-induced enhancements in arithmetic. However, it is also important to note that, in contrast to the fixed administration order of achievement tests utilized by Hillman, Pontifex et al. (2009), within the present investigation the order of the achievement tests was counterbalanced. Thus, it may be that the exercise-induced enhancements in cognition begin to wane over the course of an hour. Thus, future research is necessary to better understand the relationship between acute exercise and scholastic performance administered more closely following the bout of exercise using a measure that possesses greater sensitivity to detect more fine-grained changes in achievement. Collectively, however these findings provide support for recommendations by the National Association for Sport and Physical Education (NASPE) that short exercise bouts be incorporated during the school day as part of a comprehensive school physical activity program (NASPE, 2008), and suggest that acute bouts of exercise may have real-world implications for maximizing cognitive health and function during development while serving to transiently reduce ADHD-related impairments in academic performance (Gapin, Labban, & Etnier, 2011).

Conclusions

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The results of this investigation appear to support the use of single bouts of moderately intense aerobic physical activity as a non-pharmaceutical treatment for temporarily improving the cognitive health and effective functioning of preadolescent children with ADHD. This neurobehavioral disorder represents one of the most prevalent childhood disorders in the United States (American Psychiatric Association, 2000; Biederman, 1998; Wolraich et al., 1998), accounting for a combined total cost to public school systems exceeding $3 billion in 1995 alone (NIH, 1998). Over the course of development, ADHD has been associated with increased risks for poorer academic achievement, disciplinary problems, early substance experimentation and abuse, anxiety, depression, and difficulty maintaining employment (Barkley et al., 1993; Booth et al., 2007; Bracken & Boatwright, 2005). Further, there is a general societal concern regarding the over-diagnosis of ADHD and, in particular, the use of psychostimulants as the primary method of treatment for ADHD (Wilson & Jennings, 1996). As a result, one of the ramifications of over-diagnosis of ADHD is the exorbitant cost to our health-care system and families for long-term medication use for children who may not necessarily have ADHD. While pharmacological treatments have largely been found effective in the short-term management of the behavioral symptoms of ADHD (Solanto et al., 2001); psychostimulants only serve to ameliorate behavioral symptoms, not necessarily treatment of the root failure in inhibition, which is believed to be responsible for deficits underlying the manifestation of ADHD (Barkley, 1997). Thus, while medication use offers a temporary respite from their disorder, children may face a potential lifetime of battling it.

Accordingly, the finding that acute exercise is effective in enhancing inhibitory aspects of cognition in children with ADHD has a number of important societal implications that may help to guide future healthcare and educational policies. That is, a treatment plan that includes regular

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acute bouts of aerobic exercise may provide a unique initial treatment option for any child who may be exhibiting ADHD like symptoms, given that it has been found to relate to enhancements in inhibition and scholastic performance in healthy children as well. Further, given that changes in cognition associated with chronic physical activity participation are believed to be progressively accrued through repeated bouts of acute exercise, such a treatment plan may also serve to create more long-term changes in inhibitory control. That is, a growing body of research has begun to elucidate the beneficial effects of chronic physical activity participation leading to increased aerobic fitness has on brain health and cognition (see Hillman, Erickson, & Kramer, 2008 for review). Interestingly, results from these investigations have observed that individuals with greater physical activity/aerobic fitness exhibit a general enhancement in cognition with a disproportionately larger effect for tasks requiring greater cognitive control demands (Colcombe & Kramer, 2003; Kramer, Colcombe, McAuley, Scalf, & Erickson, 2005; Kramer et al., 1999; Pontifex et al., 2011), similar to the observed relationship between acute bouts of exercise and cognition. Further, chronic physical activity participation leading to increased aerobic fitness has also been found to relate to structural changes within the brain, with increased tissue volume in the prefrontal and temporal cortices (Colcombe et al., 2004, 2006) as well as portions of the basal ganglia and hippocampus (Chaddock, Erickson, Prakash, Kim et al., 2010; Chaddock, Erickson, Prakash, VanPatter et al., 2010); in addition to functional enhancements in neural processes related to the allocation of attentional resources (Hillman, Buck, Themanson, Pontifex, & Castelli, 2009; Pontifex, Hillman, & Polich, 2009; Pontifex et al., 2011), response conflict (Pontifex et al., 2011), and greater integrity of action monitoring processes (Pontifex et al., 2011; Themanson & Hillman, 2006; Themanson, Hillman, & Curtin, 2006; Themanson, Pontifex, & Hillman, 2008). Given that these neural structures and processes mirror those which exhibit

deficits in children with ADHD (Aylward et al., 1996; Barry et al., 2003; Castellanos et al., 1996, 2001; Dimoska et al., 2003; Filipek et al., 1997; Giedd et al., 1994; Hynd et al., 1991; Johnstone & Barry, 1996; Jonkman et al., 2000; Kemner et al., 1996; Liotti et al., 2005, 2007; Pliszka et al., 2000; Rubia et al., 1999; van Meel et al., 2007; Wiersema et al., 2006; Yeo et al., 2003), over the course of repeated bouts of acute aerobic exercise, these neuronal structures and processes may be sufficiently enhanced to more permanently treat the underlying etiology of ADHD (Gapin et al., 2011). Further research is necessary in this area; however, to better understand how acute bouts of exercise combine and compare with other more traditional ADHD treatment strategies and how chronic physical activity participation serves to influence children with ADHD.

　　　To better understand the relationship between physical activity and cognition, research has attempted to examine the cellular and molecular cascades that are triggered by physical activity in non-human animal models (which in humans can only be indirectly examined and inferred), as well as the structural and functional manifestations of changes in cognition resulting from physical activity in humans. Thus, this research has allowed for speculation regarding some of the possible mechanisms underlying acute exercise-induced enhancements in cognition. One such mechanism that has been postulated as being involved in this relationship are neurotrophic factors such as insulin-like growth factor (IGF1) and brain derived neurotrophic factor (BDNF), which have been implicated in chronic physical activity induced increases in angiogenesis (i.e., the creation of new capillaries), neurogenesis (i.e., the creation of new neurons), cellular proliferation, and neural plasticity (Brezun & Daszuta, 2000; Russo-Neustadt, Ha, Ramirez, & Kesslak, 2001; van Praag, Kempermann, & Gage, 1999; Vaynman & Gomez-Pinilla, 2005). Interestingly, in non-human animal models, the upregulation of BDNF associated with chronic

exercise occurred after only 3 bouts of exercise (Molteni, Ying, & Gomez-Pinilla, 2002). While, in humans, previous research has observed intensity dependent increases in circulating serum concentrations of BDNF after acute physical activity participation (Ferris, Williams, & Shen, 2007). Further, hippocampal neurogenesis, and associated increases in learning and memory, has been found to reach its maximum in non-human animal models after only two weeks of an exercise intervention (Periera et al., 2007). Consequently, these neural modulations, coupled with exercise-induced facilitations in microglia and astrocytes (Ehninger & Kempermann, 2003), may contribute to enhancing cognition following a single bout of exercise.

Another possible mechanism, which has been posited as underlying acute exercise-induced enhancements in cognition, is increases in cerebral blood flow (see Querido & Sheel, 2007 for review). That is, previous findings from non-human animal models have observed that physical activity participation serves to increase cerebral blood flow to specific neural regions involved in locomotion, equilibrium, cardiorespiratory control, and areas of the hippocampus (Delp et al., 2001; Pereira et al., 2007). Thus, these exercise-induced increases in cerebral blood flow may serve to enhance neural function by supplying greater metabolic resources and removing metabolic waste from these regions. Another intriguing mechanism underlying these acute-exercise induced enhancements may be that acute-exercise serves to modulate aspects of the default-mode network. Research into the default mode network has exploded in recent years with findings suggesting that functional interconnectivity among neural regions relates to aspects of cognitive health (Miller et al., 2008; Voss, Erickson et al., 2010). Although to date no prior research has investigated the extent to which this default-mode network may be sensitive to acute bouts of exercise, recent findings from a randomized controlled trial have indicated that a chronic exercise intervention in older adults served to enhance aspects of the default-mode

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network (Voss, Prakash et al., 2010). Accordingly, future research is clearly necessary to better address these potential mechanisms as they relate to acute exercise-induced changes in cognition.

Given the relative infancy of research in the area of acute exercise and cognition, particularly with regard to preadolescent populations, a great deal of research is still necessary to understand the specific parameters of exercise which optimize its influence on cognition and how other factors (i.e., personality, dietary intake, brain health, etc…) may relate to changes in cognition associated with acute exercise. Further, with regard to children with ADHD, the extent to which the effects observed within the current investigation generalize to children with more severe cases of ADHD or children undergoing pharmacological treatment is still unknown. Thus, future research will need to investigate these factors further to better understand the utility of acute exercise in enhancing inhibition in these populations. However, given that approximately 44% of US children with ADHD do not undergo pharmacological treatments (Biederman & Faraone, 2005); these findings do have substantial clinical utility in enhancing the cognitive health and functioning of children with ADHD. It is also important to note that we do not yet have a clear understanding of what the half-life of a bout of acute exercise is. That is, limited research in this area has investigated multiple time points following an acute bout of physical activity to examine how long exercise-induced modulations persist. Clearly, one area of future research that is much needed is to better characterize the duration of the potential benefits for cognition incurred by an acute bout of physical activity. Some insight can be gleaned from the findings of Pontifex, Hillman, Ferhall and colleagues (2009), Hillman et al. (2003) and Hillman, Pontifex et al. (2009), which suggest that a single bout of aerobic exercise relates to enhancements in inhibition and working memory and may persist for up to an hour following the cessation of exercise. However, other adaptations may persist for hours, if not days, or beyond.

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Collectively, the current investigation is the first to examine the relationship between acute bouts of aerobic exercise and inhibitory control in children with ADHD. Given that previous research has observed that children with ADHD are less likely to participate in vigorous physical activity and organized sports relative to children without ADHD (Kim, Mutyala, Agiovlasitis, & Fernhall, 2011), the current findings suggest that motivating children with ADHD to be physically active is of particular importance for both their physical and mental health. The current study further replicates and extends prior research to suggest that single bouts of aerobic exercise are effective in facilitating neural processes underlying inhibitory aspects of cognitive control in both healthy children and children with ADHD. Accordingly, these findings indicate that single bouts of moderate intensity aerobic exercise may serve as a transient non-pharmaceutical treatment option for children with ADHD to improve the cognitive health, academic performance, and overall effective functioning of this population.

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