Physical Activity and Cognitive Control: Implications for Drug Abuse

Charles H. Hillman¹ and David J. Drobes²

¹University of Illinois and ²University of South Florida

ABSTRACT—This article focuses on a growing body of research that has studied the beneficial relation between chronic participation in—and acute responses to—physical activity and brain health, cognition, and scholastic achievement. Specifically, it highlights the relevant behavioral and neuroimaging findings of this beneficial relation in children and adults, providing evidence for the influence of chronic and acute physical activity on brain structure and function that underlie cognition and scholastic achievement. In addition, the article discusses the implications for the role of physical activity on drug use, as well as its prevention and treatment, and makes recommendations for further research in this area.

KEYWORDS—fitness; exercise; attention; memory; drug use; cognition

In recent years, physical inactivity in childhood has been steadily rising (Ogden, Carroll, Curtin, Lamb, & Flegal, 2010; Ogden, Flegal, Carroll, & Johnson, 2002). The consequences of a sedentary existence are evidenced by an increasing incidence of ill health in children. Unfortunately, inactivity often continues beyond childhood, with further implications for the prevalence of ill health (e.g., cardiovascular disease, Type 2 diabetes) during adulthood. Although rarely addressed in discussions of these public health concerns, physical inactivity also has implications for brain health and cognition. That the relation between inactivity and cognitive health has not emerged as a larger societal concern is surprising, given its

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obvious relation to childhood obesity and other inactivityrelated disorders that have been steadily rising over the past three decades (Ogden et al., 2006).

Exacerbating these issues, many school districts, in an effort to improve the educational environment, have minimized or eliminated opportunities for physical activity (e.g., physical education and recess) from the school day (Sallis, 2010). This seems a curious strategy, given the growing literature that indicates the benefits of aerobic forms of physical activity to cognitive health and learning (see Hillman, Erickson, & Kramer, 2008, for review). Although not intuitive, the empirical data also indicate that time spent being physically active does not detract from scholastic performance (Ahamed et al., 2007). In fact, to the best of our knowledge, available research has not found a single instance in which physical activity interferes with achievement in core academic subject matter, with the extant literature consonant in demonstrating that physical activity and fitness are either positively related to scholastic achievement (Castelli, Hillman, Buck, & Erwin, 2007; Davis, Tomporowski, McDowell, Austin, & Miller, 2011; Donnelly et al., 2009) or unrelated to it (Ahamed et al., 2007; Dwyer, Coonan, Leitch, Hetzel, & Baghurst, 1983). Regardless of the outcome, the collective findings indicate that time spent engaged in physical activity does not detract from academic goals, and at the very least, might positively impact the physical health of the learner. In spite of the apparent relation between physical activity and scholastic achievement, few studies employed causal designs to examine the effects of physical activity on cognition in children. A meta-analysis of these studies observed a positive relation (ES = .32) between physical activity and cognition generally, as well as a beneficial relation between physical activity and cognitive processes that subserve scholastic performance (Sibley & Etnier, 2003).

Furthermore, there is growing evidence that physical inactivity during childhood and adolescence is associated with substance-use experimentation and risk for later addiction. Interestingly, both physical activity and substance use have

Correspondence concerning this article should be addressed to Charles H. Hillman, Department of Kinesiology and Community Health, 317 Louise Freer Hall, 906 South Goodwin Avenue, University of Illinois, Urbana, IL 61801; e-mail: chhillma@illinois.edu.

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been linked to a number of changes in brain structure and function, and they have also been linked to similar brain structures and overlapping networks. Specifically, a beneficial relation has been observed between physical activity and regions of the brain that subserve aspects of memory (i.e., hippocampus) and cognitive control (e.g., prefrontal cortex, anterior cingulate cortex, parietal cortex). Cognitive control refers to a subset of goal-directed, self-regulatory processes associated with the control of thought and action. Core cognitive processes collectively termed cognitive control include inhibition, working memory, and cognitive flexibility (Miyake et al., 2000). At the same time, substance use has been linked to long-term alterations in brain structures and pathways considered critical for reward processing, judgment and decision making, learning and memory, and cognitive control (e.g., mesolimbic and mesocortical pathways, prefrontal cortex, hippocampus, anterior cingulate). Given that similar brain structures are influenced by physical activity and substance use, a natural question arises concerning whether or not physical activity may serve to ameliorate or protect against substance abuse. After we review the evidence linking physical activity with brain health and cognition, we discuss implications of this research for the understanding, prevention, and treatment of addictive behavior. In this regard, we note that the role for physical activity may not be uniform across developmental stages, with certain potential mechanisms of action being more relevant to risk for early drug use or experimentation, and others being more pertinent for engrained patterns of heavy drug use or addiction.

FITNESS AND BRAIN STRUCTURE

A growing body of cross-sectional research with children has demonstrated differences in brain structure and function related to low cardiorespiratory fitness. Despite the cross-sectional nature of this work, researchers have been careful to yoke individuals with different fitness levels on various factors known to influence fitness and cognition (e.g., age, gender, socioeconomic status, pubertal timing, intelligence, etc.) when placing participants into fitness groupings (e.g., Hillman, Buck, Themanson, Pontifex, & Castelli, 2009; Hillman et al., 2009; Pontifex et al., 2011). Accounting for such variables is important when investigating the relation of physical activity or fitness to cognition in children, because factors such as age, gender, and intelligence have been related to cognition, independent of physical activity (e.g., Hillman et al., 2006; Mezzacappa, 2004).

In two studies, Chaddock, Erickson, Prakash, Kim, et al. (2010) and Chaddock, Erickson, Prakash, VanPatter, et al. (2010) found cardiorespiratory fitness and the volume of specific brain structures to be linked to aspects of memory and cognition. In the first study, Chaddock, Erickson, Prakash, Kim, et al. (2010) placed 9- to 10-year-old children into low- and high-fitness groupings based on VO₂max values (measures of maximal oxygen consumption, the gold standard of cardiorespiratory

fitness). Using magnetic resonance imaging (MRI), the researchers found smaller bilateral hippocampal volume in low-fit children. Furthermore, low-fit children performed more poorly on a test of relational memory, which is mediated by the hippocampus (Cohen & Eichenbaum, 1993; Cohen et al., 1999), although no differences emerged on a test of item memory, which is supported by structures outside the hippocampus. In addition, hippocampal volume was positively related to performance on the relational memory task but not on the item memory task, and bilateral hippocampal volume was observed to mediate the relation between fitness and relational memory (Chaddock, Erickson, Prakash, Kim, et al., 2010). Such findings are consistent with both behavioral indices of relational memory in preadolescent children (Chaddock, Hillman, Buck, & Cohen, 2011) and neuroimaging findings in elderly adults (Erickson et al., 2009) and support the robust rodent literature demonstrating exercise-effects on cell proliferation (van Praag, Christie, Sejnowski, & Gage, 1999) and survival (Neeper, Gomez-Pinilla, Choi, & Cotman, 1995) in the hippocampus that relate enrichment of learning and memory.

In the second study by Chaddock, Erickson, Prakash, Van Patter, et al. (2010), a similar comparison between 9- and 10year-olds in low- and high-fitness groups yielded differential findings for the basal ganglia, a subcortical structure involved in the interplay of cognition and willed action. Specifically, compared to high-fit children, low-fit children exhibited less volume in the dorsal striatum (i.e., caudate nucleus, putamen, globus pallidus), but showed no fitness-related differences in the ventral striatum. Such findings are not surprising given the role of the dorsal striatum in cognitive control and response resolution (Aron, Poldrack, & Wise, 2009; Casey, Getz, & Galvan, 2008), as well as the growing body of research in children and adults indicating that lower amounts of fitness are associated with poorer control of attention, memory, and cognition (Colcombe & Kramer, 2003; Etnier & Chang, 2009; Hillman et al., 2008). Chaddock, Erickson, Prakash, VanPatter, et al. (2010) further observed that low-fit children exhibited a decreased ability to manage perceptual interference engendered by a flanker task, which requires variable amounts of inhibitory control and response resolution, and that lower basal ganglia volume was related to poorer response resolution. Such findings indicate that the dorsal striatum is involved in these aspects of higher order cognition, and that fitness may influence cognitive control during preadolescent maturation.

Similar findings have been found in both cross-sectional (Colcombe et al., 2003; Erickson et al., 2011) and longitudinal, randomized (Colcombe et al., 2006; Erickson et al., 2009) studies of older adults. Specifically, aging is accompanied by reductions in gray and white matter in the frontal, temporal, and parietal cortices (Colcombe & Kramer, 2003), as well as by reductions in subcortical structures such as the hippocampus (Erickson et al., 2009). However, physical activity has been related to a lessening in the amount of reduction observed in these brain regions (Colcombe & Kramer, 2003; Erickson et al., 2009), with longitudinal, randomized trials indicating that 6 months of physical activity lead to increases in aerobic fitness yield increases in gray and white matter volume in the prefrontal and temporal cortices (Colcombe et al., 2006) and the hippocampus (leading to improvements in spatial memory; Erickson et al., 2009). Such findings suggest that physical activity is associated with the sparing of specific brain tissue during aging, and highlight the need for research using causal designs to better understand the relation of physical activity to cognitive development.

FITNESS AND BRAIN FUNCTION

Other research has attempted to characterize fitness-related differences in brain function using functional MRI (fMRI) and event-related brain potentials (ERPs). In the only published fMRI investigation of childhood physical activity to date, Davis et al. (2011) studied 20 sedentary, overweight 7- to 11-year-olds who had been randomly assigned to an intervention group that exercised daily or to a nonactivity control group. After approximately 14 weeks, fMRI data collected during an antisaccade task (which involves moving the eye in the opposite direction of a presented stimulus and thus requires inhibition and attentional control) showed greater bilateral activation of the prefrontal cortex in the intervention group and decreased bilateral activation of the posterior parietal cortex (a region involved in the reorienting of visual-spatial attention). Such findings indicate that physical activity may improve attentional control and inhibition, and illustrates where some of the differences in brain function may lie.

Other imaging research has examined the neuroelectric system (i.e., ERPs) to investigate which cognitive processes occurring between stimulus engagement and response execution are influenced by cardiorespiratory fitness or single bouts of aerobic exercise. Several studies (Hillman, Castelli, & Buck, 2005; Hillman et al., 2009; Pontifex et al., 2011) have examined the P3 component of the stimulus-locked ERP and demonstrated that low-fit preadolescent children had smaller amplitude and longer latency ERPs than did their high-fit peers. Contemporary theory suggests that P3 relates to neuronal activity associated with the revision of the mental representation of the previous event within the stimulus environment (Donchin, 1981). P3 amplitude reflects the allocation of attentional resources when working memory is updated (Donchin & Coles, 1988), such that P3 is sensitive to the amount of attentional resources allocated to a stimulus (Polich, 1987; Polich & Heine, 1996). P3 latency is generally considered to represent stimulus evaluation and classification speed (Duncan-Johnson, 1981; Kutas, McCarthy, & Donchin, 1977), and thus may be considered a measure of stimulus detection and evaluation time (Ilan & Polich, 1999; Magliero, Bashore, Coles, & Donchin, 1984). Accordingly, the findings suggest that low-fit children allocate fewer attentional resources

and have slower stimulus classification speed relative to high-fit children (Hillman et al., 2005; Hillman et al., 2009), with additional research suggesting that low-fit children also demonstrate less flexibility in the allocation of attentional resources, as indexed by the modulation of P3 amplitude (Pontifex et al., 2011). Given that low-fit children also demonstrate lower task performance, the P3 component appears to reflect deficits in aspects of cognition that relate to willed action (Hillman et al., 2009; Pontifex et al., 2011). In an extension of these findings, Hillman et al. (2009) found that single bouts of exercise had transient benefits to cognition in a sample of 9- to 10-year-olds (regardless of fitness), such that they had larger P3 amplitude, shorter P3 latency, and greater task performance after 20 min of treadmill walking than after 20 min of seated rest. Importantly, these findings extended to scholastic performance, with children performing better on an academic achievement test preceded by exercise rather than by rest (Hillman et al., 2009).

These ERP studies (Hillman et al., 2009; Pontifex et al., 2011) have also focused on aspects of cognition involved in action monitoring, investigating the error-related negativity (ERN) component in low- and high-fit children. The ERN, observed in response-locked ERP averages, is often elicited by commission errors during a task and is believed to represent either the detection of errors during task performance (Gehring, Goss, Coles, Meyer, & Donchin, 1993; Holrovd & Coles, 2002) or, more generally, the detection of response conflict (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Yeung, Cohen, & Botvinick, 2004), which oftentimes is engendered by the commission of an error. The ERN potential is thought to have a single neural generator located at, or near, the dorsal portion of the anterior cingulate cortex (Carter et al., 1998; Dehaene, Posner, & Tucker, 1994; Miltner et al., 2003). Relative to fitness, low-fit children have larger ERN amplitude during rapid response tasks (Hillman et al., 2009), but are less flexible in the allocation of these resources during tasks that impose variable action monitoring demands, as evidenced by changes in ERN amplitude for high-fit children and no modulation of ERN in low-fit children (Pontifex et al., 2011). Collectively, such a pattern of results may indicate that low-fit children allocate fewer attentional resources during stimulus engagement (P3 amplitude), but increase activation of resources involved in the monitoring of their actions (ERN amplitude). Alternatively, high-fit children allocate greater resources toward environmental stimuli and demonstrate less reliance upon action monitoring (only increasing resource allocation to meet the demands of the task). Under more demanding task conditions, low-fit children's strategy appears to fail, because they perform more poorly under conditions of greater response conflict. For more in-depth discussion the interested reader is directed to several reviews that provide a mechanistic understanding of the relation of physical activity to brain structure and function using nonhuman animal models (e.g., Erickson & Kramer, 2007; Hillman et al., 2008; Vaynman & Gomez-Pinilla, 2006).

PHYSICAL ACTIVITY AND DRUG ABUSE

We have discussed research linking both chronic and acute physical activity to brain health during childhood and beyond. Overall, there is evidence that physical activity is related to improved cognitive function, and the neural basis for these effects has been delineated. Although much of the available evidence pertaining to children is cross-sectional, recent studies have included a number of relevant controls, and a growing number of longitudinal studies of adults are supportive of the cross-sectional findings. Importantly, brain structures affected by physical activity are closely related to cognitive control, such as those involved in effortful decision making or planning of thoughts or actions. In this section, we will first briefly review findings regarding the association between physical activity and drug use. Given the effects of physical activity on cognitive control, we will next discuss recent models of drug use and addiction that emphasize these processes. Finally, we will consider physical activity for its potential contribution to the prevention and treatment of drug abuse via its influence on cognitive control.

Concern about inactivity during childhood is amplified by growing evidence of a relation between physical activity and drug use or abuse. Much of the evidence for this relation is cross-sectional or correlational in nature. For instance, children who are more physically active are less likely to engage in substance use experimentation (Moore & Werch, 2005) or to develop problems with use and abuse of various drugs during adolescence or later. Both cross-sectional and longitudinal designs have been used to demonstrate that adolescents who engage in team sports are less likely to smoke cigarettes (e.g., Metzger, Dawes, Mermelstein, & Wakschlag, 2011) or engage in alcohol and other drug use (e.g., Terry-McElrath, O'Malley, & Johnston, 2011). In one study, high school students who were engaged in team sports showed a negative correlation between physical activity and the progression of smoking behavior from 9th to 12th grades (Audrain-McGovern, Rodriguez, Wileyto, Schmitz, & Shields, 2006). It is difficult to conclude that physical activity, per se, is responsible for these benefits. Other features of team sports-such as engagement in prosocial and esteem-building activities, presence of adult supervision, stress reduction, or reduction in idle time-may play a role. Nonetheless, a consistent finding is that children and adults who are more physically active are less likely to engage in drug use behavior.

Although little direct evidence supports a causal effect of activity on drug use in humans, several animal studies have examined the effects of exercise on drug intake or its effects. In one study, rats that exercised on a running wheel for 6 weeks were less likely to self-administer cocaine using a progressive ratio reinforcement schedule than were sedentary rats (Smith, Schmidt, Iordanou, & Mustroph, 2008). Other studies have reported similar findings of chronic exercise-related reductions in alcohol consumption (Hammer, Ruby, Brager, Prosser, & Glass, 2010) or alcohol intoxication (Leasure & Nixon, 2010). Thus, there is experimental support for the proposition that exercise-based intervention may reduce drug use.

In humans, recent studies with adult cigarette smokers provide strong evidence that acute exercise can reduce drug-related motivation. Several experimental designs have been used to demonstrate that various forms of exercise can reduce cravings to smoke and nicotine-withdrawal symptoms (see review by Taylor, Ussher, & Faulkner, 2007). Importantly, exercise has also been shown to acutely reduce ad-lib smoking behavior (Taylor & Katomeri, 2007), and two studies indicate that the motivation to smoke upon exposure to salient smoking-related cues is reduced immediately following a single bout of cardiovascular exercise (Elibero, Janse Van Rensburg, & Drobes, 2011; Taylor & Katomeri, 2007). Finally, a recent study demonstrated that exercise-induced reductions in cue-elicited cigarette craving were associated with reduced activation in brain areas involved with reward processing, along with increased activation in areas related to cognitive control (Janse Van Rensburg, Taylor, Hodgson, & Benattavallah, 2009). Overall, these laboratory studies suggest that physical activity may confer benefits among established (addicted) drug users that make it easier to avoid drug use, and it appears that these benefits may be associated with increased activation of cognitive control brain mechanisms. Importantly, it is not known if these direct effects of exercise on smoking-related motivation would operate in a similar fashion among smokers or other drug users during experimental stages of drug use. Nonetheless, it is interesting to speculate that the development of exercise habits in early (predrug) developmental periods may carry a protective effect once experimentation begins, which could offset development of the addictive process. Clearly, further research is needed to corroborate these effects across various stages of drug use.

As we have discussed, neural mechanisms that support cognitive control appear to be strengthened through physical activity. Several prominent models of drug addiction emphasize failures of cognitive control (e.g., Bechara, 2005; Hyman, 2005; Kalivas & Volkow, 2005). In general, neural activation associated with cognitive control (dorsolateral and medial prefrontal cortex, anterior cingulate cortex) is thought to be necessary to counteract activation in posterior cortical and subcortical regions that are considered important for drug-related reward processing (e.g., caudate, putamen, nucleus accumbens; Kalivas & Volkow, 2005). Thus, because a frequent drug user may become sensitized to the reinforcing effects of drugs (Robinson & Berridge, 1993), deficient cognitive control mechanisms can lead to decreased self-regulatory behavior, thereby affecting the desire for further drug intake. In contrast, intact cognitive control decreases the tendency to act impulsively (decreasing the likelihood that drug use will occur). Given its effects on brain function, exercise may be well suited for counteracting drug-taking behavior (via improved cognitive control). To be clear, although evidence discussed above supports a role of physical activity for reducing craving, the most pertinent neural processes may be those that bolster one's ability to counter (or resist acting upon) the desire to use drugs (see Tiffany, 1990).

The discussion above implies that physical activity can strengthen cognitive control processes as a countering force to heavy or addicted drug users' motivation to use drugs. It is also important to note that physical activity may play an important role for nonaddicted individuals (or nonusers) at earlier developmental stages. Indeed, a well-functioning cognitive control system may be a key determinant in suppressing impulsive decisions that can lead to early or experimental drug use. As such, cognitive control systems that are positively affected by physical activity may have relatively distinct functional roles in avoiding (among adolescents) or reducing (among older or ongoing users) drug use at different developmental stages.

The role of cognitive control in drug use initiation or ongoing drug addiction may be especially relevant for those with premorbid deficits in these neurally mediated processes. In particular, cognitive control dysfunction is pronounced in several neuropsychiatric disorders that carry a disproportionate rate of comorbid substance use disorders, such as schizophrenia, depression, and attention deficit hyperactivity disorder. An important factor that may motivate drug use among individuals with these disorders is the desire to counter (or self-medicate) their cognitive deficits with drugs that appear to have at least temporary facilitative effects on cognitive function, including nicotine (see Evans & Drobes, 2009). Thus, physical activity may be valuable for preventing drug use among individuals with premorbid neurocognitive dysfunction, or as a treatment component for individuals with comorbid drug use disorders. The acute and/or chronic effects of exercise on cognitive control may reduce the need to self-medicate deficient cognitive processing.

FUTURE DIRECTIONS

As we have discussed, physical activity is associated with improved cognitive control and memory, and there appears to be a neural basis for these effects. However, other possibilities for the observed benefits of physical activity to brain health and cognition exist, including personality (e.g., motivation), demographic (e.g., socioeconomic status), and genetic factors. In addition, the cross-sectional nature of many of the child studies leaves open the possibility that children who perform better in their academic courses may derive benefits from their participation in physical activities. Given the role of cognitive control in drug use and addiction, there are several avenues to explore as far as optimizing physical activity in a preventative or interventional fashion to address drug use and abuse. First, the general benefits of physical activity on brain health and cognition should be emphasized in educational programming, because their relation with reduced drug taking (among many positive outcomes) has been clearly demonstrated. Second, greater identification of high-risk youth based on cognitive control indices may facilitate targeted application of physical activity as a preventative measure. Third, youth who engage in early experimentation with drugs, or who are developing more serious patterns of chronic or problematic use, should be candidates for comprehensive intervention. The findings we have reviewed here suggest that physical activity may provide an acute coping tool or a long-term strategy to improve cognitive control and thus decrease the susceptibility for development or continuation of a drug abuse problem.

SUMMARY

Physical activity and aerobic fitness appear to positively benefit cognition and its neural underpinnings, resulting in improved scholastic performance in children. In addition, significant overlap exists between brain regions that are influenced by physical activity and drug use or abuse and that comprise a network that mediates cognitive control function. Future research must examine the efficacy of physical activity in reducing initiation and/or continuation of drug-taking behavior, and much work will be needed to delineate the optimal activity parameters (e.g., form, intensity, chronicity, timing) and integration within existing drug-abuse prevention and treatment programs. Regardless, physical activity is an important health behavior required for the successful growth and maturation of brain structure and function. In a time when industrialized nations are challenged with a growing propensity to engage in sedentary behaviors, it is more important than ever to understand the positive effects of physical activity for brain, cognition, and substance use to better promote lifelong cognitive health and learning.

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