

III. THE IMPORTANCE OF PHYSICAL ACTIVITY AND AEROBIC FITNESS FOR COGNITIVE CONTROL AND MEMORY IN CHILDREN

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ABSTRACT In this chapter, we review literature that examines the association among physical activity, aerobic fitness, cognition, and the brain in elementary school children (ages 7–10 years). Specifically, physical activity and higher levels of aerobic fitness in children have been found to benefit brain structure, brain function, cognition, and school achievement. For example, higher fit children have larger brain volumes in the basal ganglia and hippocampus, which relate to superior performance on tasks of cognitive control and memory, respectively, when compared to their lower fit peers. Higher fit children also show superior brain function during tasks of cognitive control, better scores on tests of academic achievement, and higher performance on a real-world street crossing task, compared to lower fit and less active children. The cross-sectional findings are strengthened by a few randomized, controlled trials, which demonstrate that children randomly assigned to a physical activity intervention group show greater brain and cognitive benefits compared to a control group. Because these findings suggest that the developing brain is plastic and sensitive to lifestyle factors, we also discuss typical structural and functional brain maturation in children to provide context in which to interpret the effects of physical activity and aerobic fitness on the developing brain. This research is important because children are becoming increasingly sedentary, physically inactive, and unfit. An important goal of this review is to emphasize the importance of physical activity and aerobic fitness for the cognitive and brain health of today's youth.

An active lifestyle during childhood is beneficial to physical, cognitive, and brain health. Physical activity helps prevent chronic diseases such as obesity, certain cancers, type 2 diabetes, and coronary heart disease throughout the lifespan (CDC, 2009; USDHHS, 2008). More recently, physical activity has been

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associated with enhanced cognitive function using neuropsychological and psychometric tests (Buck, Hillman, & Castelli, 2008; Chaddock, Hillman, Buck, & Cohen, 2011; Sibley & Etnier, 2003). Physical activity and higher levels of aerobic fitness have also been found to be associated with better academic performance (see Chapter 7; Castelli, Hillman, Buck, & Erwin, 2007; Chomitz et al., 2009; Coe, Pivarnik, Womack, Reeves, & Malina, 2006; see CDC, 2010; Shepherd, Pintado, & Bean, 2011; Singh, Uijtdewilligen, Twisk, van Mechelen, & Chinapaw, 2012; Trudeau & Shephard, 2008 for reviews). The performance differences of higher and lower fit children have been associated with differences in structural brain volumes using magnetic resonance imaging (MRI; Chaddock, Erickson, Prakash, Kim, et al., 2010; Chaddock, Erickson, Prakash, VanPatter, et al., 2010) as well as brain function, which has been measured by event-related brain potentials (ERPs; Hillman, Buck, Themanson, Pontifex, & Castelli, 2009; Hillman, Castelli, & Buck, 2005; Pontifex et al., 2011) and functional MRI (fMRI; Chaddock, Erickson, et al., 2012; Davis et al., 2011; Voss et al., 2011).

This research is important because physical activity is decreasing in and out of the school environment (Troiano et al., 2008; see Chapter 2), and children are becoming increasingly sedentary, unfit, and overweight (CDC, 2009). As a result, children in today's society have a greater likelihood of poor health (CDC, 2009). Here, we review literature that demonstrates a positive relationship between physical activity, aerobic fitness, cognition and the brain in elementary school children (ages 7–10 years). An important goal of this review is to demonstrate the effectiveness of physical activity in leading to gains in cognition as well as physical and brain health.

THE DEVELOPING BRAIN, COGNITIVE CONTROL, AND MEMORY

To study the relationship between physical activity and neurocognitive health during childhood, it is important to understand changes in cognition during development, the neural mechanisms supporting these changes, and the role of experience. An understanding of typical development and plasticity provides an important context in which to interpret the effects of physical activity, aerobic fitness, and other lifestyle factors on the developing brain. For example, obesity and inactivity have been found to relate to poorer developmental outcomes (see Chapter 4), whereas aerobic fitness, intellectual stimulation (e.g., computerized training, noncomputerized games), martial arts, and yoga/mindfulness are associated with positive outcomes (Diamond & Lee, 2011).

The following discussion provides a brief overview of structural and functional brain maturation, specifically highlighting the development of cognitive control and memory (Gathercole, 1998; Ghetti & Bunge, 2012;

Gogtay et al., 2004). These cognitive constructs are the focus of this review given their established association with physical activity and aerobic fitness across the lifespan as well as their importance for school achievement and success on everyday challenges.

Cognitive control (also known as “executive control”) refers to cognitive processes associated with the control of thought and action and the ability to guide behavior toward specific goals and formulate decisions. These functions include: (1) selective attention to relevant information and the filtering of distracting information (selective attention and interference suppression); (2) inhibition of inappropriate response tendencies (response inhibition); (3) flexibly switching between tasks and restructuring knowledge and information based on changing situational demands (task-switching); (4) the ability to temporarily store and manage information while learning and performing cognitive challenges (working memory); (5) working with information held in working memory (manipulation); and (6) using context to determine whether an action is appropriate or a thought is relevant (task-set representation) (Bunge & Crone, 2009; Miyake et al., 2000). These cognitive skills have been found to relate to academic achievement during childhood (Bull & Scerif, 2001; DeStefano & LeFevre, 2004; St. Clair-Thompson & Gathercole, 2006).

Over the course of childhood and adolescence, cognitive control improves, and these improvements are said to parallel the structural and functional development of the brain, especially with regard to brain circuits, which include frontal, striatal, and parietal brain regions (Bunge & Crone, 2009). The frontal cortex, through its extensive connections with various cortical and subcortical structures, is implicated in attention, interference control, response inhibition, and the selection, maintenance, and manipulation of task-relevant information within working memory (Banich et al., 2000; Hazeltine, Poldrack, & Gabrieli, 2000; Liddle, Kiehl, & Smith, 2001; Olesen, Westerberg, & Klingberg, 2003). The frontal cortex projects to the basal ganglia, a group of subcortical structures subdivided into the dorsal striatum, which is implicated in cognitive control, motor control, response selection and resolution, and the execution of learned behaviors, and the ventral striatum, part of an affect and reward pathway involved in reinforcement and motivation (Aron, Poldrack, & Wise, 2009). The parietal cortex is also thought to play a role in cognitive control, specifically selective spatial attention (Corbetta, Kincade, & Shulman, 2002; de Fockert, Rees, Frith, & Lavie, 2004; Mayer, Dorflinger, Rao, & Seidenberg, 2004), maintenance of information (Banich et al., 2000; Corbetta et al., 2002; Pollmann & von Cramon, 2000), and manipulation of items in working memory (Crone & Ridderinkhof, 2011; Olesen, Nagy, Westerberg, & Klingberg, 2003).

In addition to working memory, an element of memory that is a focus of this review is relational or declarative memory, supported by the hippocampus,

its surrounding medial temporal lobe (MTL) cortices, and their interconnections with multiple cortical processing regions (Cohen & Eichenbaum, 1993; Davachi, 2006; Eichenbaum & Cohen, 2001). This system is critical to the learning and remembering of the spatial, temporal, and associative relations among multiple items, which includes all manner of relations among the constituent elements of scenes or events, as well as relations among multiple scenes or events; this circuit supports recollection of details about specific, experienced events (episodic memory; Tulving, 1972) as well as the flexible use of relational memories in novel situations (Buckner, 2009; Cohen & Eichenbaum, 1993; Eichenbaum & Cohen, 2001; Eichenbaum, Yonelinas, & Ranganath, 2007; Hannula, Ryan, Tranel, & Cohen, 2007; Hassabis, Kumaran, Vann, & Maguire, 2007; Hollup, Kjelstrup, Hoff, Moser, & Moser, 2001; Konkel & Cohen, 2009; Maguire, Frackowiak, & Frith, 1997; Maguire et al., Maguire et al., 1998, 2000; Ryan, Althoff, Whitlow, & Cohen, 2000; Schacter & Addis, 2009). The acquisition of relational knowledge is also central to scholastic achievement, and the flexible expression of memory provides a foundation for success in handling real-world challenges outside of the school environment.

STRUCTURAL BRAIN CHANGES DURING DEVELOPMENT

Several MRI studies have mapped the neuroanatomical course of normal brain development. In general, gray matter volume, which consists of neurons, glia, and capillaries, is said to follow a nonlinear curve during development (Giedd et al., 1999), with frontal, parietal, and temporal lobes generally showing a pre-pubertal increase, followed by a post-pubertal loss (Giedd et al., 1999; Sowell et al., 2003; Sowell, Thompson, Holmes, Jernigan, & Toga, 1999; Sowell, Thompson, Tessner, & Toga, 2001). The process of gray matter loss is said to begin in the dorsal parietal cortices, particularly the primary sensorimotor areas, and then spreads rostrally over the frontal cortex and caudally and laterally over the parietal, occipital, and finally the temporal cortex, with the prefrontal and lateral temporal cortices maturing last (Gogtay et al., 2004). There is little research on the developmental trajectory of the basal ganglia, yet some studies suggest a nonlinear developmental curve, with increases in volume during childhood followed by volume loss around puberty (Toga, Thompson, & Sowell, 2006). Temporal lobe gray matter structures, which include the hippocampus, are said to show nonlinear increases and decreases in volume during childhood and adolescence (Sowell, Delis, Stiles, & Jernigan, 2001; Toga et al., 2006). In a study in which individuals between aged 4–25 years completed MRI scans every 2 years, for 6–10 years, structural development of specific subregions of the hippocampus was found to be heterogeneous, with increased volume over time in the posterior hippocampus and decreased volume over time in the anterior hippocampus (Gogtay et al., 2006).

Structural brain changes likely reflect interplay among changes in cell proliferation and apoptosis, dendritic branching and pruning, and synaptic formation and elimination, in accord with the strengthening of relevant neural connections and the pruning of inefficient pathways (Andersen, 2003). Some investigators hypothesize that intra-cortical myelination might also play a role in gray matter reductions across development (Paus, 2005). White matter, composed of myelinated axons, has been found to increase roughly linearly throughout childhood (Schmithorst & Yuan, 2010). For example, tracts that connect frontal, parietal, motor, and striatal regions have shown increased white matter microstructure across development (e.g., Barnea-Goraly et al., 2005; Bonekamp et al., 2007; Chaddock-Heyman et al., 2014; Schmithorst, Wilke, Dardzinski, & Holland, 2002; see Schmithorst & Yuan, 2010, for review).

FUNCTIONAL BRAIN CHANGES DURING DEVELOPMENT

Researchers also use fMRI to examine the maturational trajectories underlying developing cognitive skills. Blood oxygen level dependent (BOLD) response is the dependent measure of most fMRI studies, which refers to the microvascular response in blood flow resulting from fluctuations in the metabolic needs of neurons as they become involved in computations, which underlie performance of tasks. Brain activation is often measured during performance of cognitive tasks, and the activation patterns are correlated with age and task performance. The adult model of brain function is often used as the “mature” or “optimal” model to which the patterns of children and adolescents are compared (Luna, Padmanabhan, & O’Hearn, 2010). Studies of the development of cognitive control in children report a variety of results, but generally suggest that children show different activation patterns to support behavioral demands compared to adults.

A number of developmental studies of brain activation during tasks of cognitive control examine attention, response inhibition (e.g., Go/NoGo, flanker, antisaccade tasks) (Diamond, 2006) and working memory (e.g., n-back, visual spatial working memory) (Baddeley, 1986; Bunge & Crone, 2009). Across childhood, there are continued improvements in these measures of cognitive control, and the frontal cortex is said to play a primary role in performance changes. Although there is additional involvement from parietal, temporal, and subcortical regions during control tasks; most developmental fMRI studies of cognitive control have mainly focused on frontal areas (Luna et al., 2010). Evidence of late structural changes in the frontal cortex makes this region especially important for understanding cognitive development (Gogtay et al., 2004).

During tasks of attention and response inhibition, the majority of studies of cognitive control across development report increased frontal activity in

children relative to adults (e.g., Booth et al., 2003; Casey et al., 1997; Durston et al., 2002; Velanova, Wheeler, & Luna, 2008). For example, Booth et al. (2003) showed increased brain activation in children (age 9–12) in fronto-striatal areas relative to adults (age 20–30) during a Go/NoGo task, and these activation differences were coupled with inferior task performance by the children. Durston et al. (2002) also showed increased activity for children (age 6–10) in the dorsal and ventral prefrontal cortex and parietal cortex during a Go/NoGo paradigm relative to adults (mean age of 28 years), and task performance positively correlated with age. Further, Velanova et al. (2008) showed increased activity in the right dorsolateral prefrontal cortex and anterior cingulate cortex in children (age 8–12) compared to adults (age 18–27) during an antisaccade task of response inhibition, coupled with lower task performance in the children. These patterns of developmental differences may indicate that children use prolonged computational processes, which may generate increased activation, but still do not allow performance at an adult level.

Whereas these studies suggest that the neural mechanisms that support cognitive control are available during childhood, but are immature or less efficient than the adult system (Booth et al., 2003; Durston et al., 2002; Velanova et al., 2008), other studies show different patterns of age-related differences in activation. Specifically, one study that examined brain function during a flanker Go/NoGo task of interference suppression and response inhibition reported that children (age 8–12) did not activate a region of the right ventrolateral prefrontal cortex that adults (age 19–33) recruited to perform tasks of cognitive control at higher levels of performance (Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002). These findings suggest that less mature task performance during childhood may relate to an inability to activate brain regions important for adult-like task performance. Additional studies of inhibitory control suggest both increases *and* decreases in activation in specific frontal regions with age (Tamm, Menon, & Reiss, 2002). For instance, a Go/NoGo study in 8- to 20-year-olds showed age-related decreases in activation in the left inferior frontal gyrus, coupled with age-related increases in activation in the left superior and middle frontal gyrus (Tamm et al., 2002). Participants across all ages did not significantly differ in task performance. Accordingly, the authors concluded that increases in middle frontal gyrus activation with age may reflect improved inhibitory processes, while decreases in inferior frontal gyrus activation with age reflect decreased effortful attention required to exert inhibitory control. To complement the findings of Tamm et al. (2002), a longitudinal study by Durston et al. (2006) suggested a developmental increase in Go/NoGo performance from 9 to 11 years of age, coupled with increased focal activation in ventral prefrontal regions (i.e., right inferior frontal gyrus) related to task performance and attenuated activation in the dorsolateral prefrontal cortex

(i.e., middle frontal gyrus, precentral gyrus, superior frontal gyrus, posterior cingulate gyrus, superior temporal gyrus) where activation was not correlated with task performance (Durston et al., 2006). The researchers suggested an increase in activation in brain areas associated with enhanced inhibitory control performance and an attenuation of brain areas not critically involved in task performance.

In addition to changes related to attention and inhibition, brain function involved in working memory is also said to change with age (Bunge & Wright, 2007). For example, fMRI activation in the superior frontal sulcus and intraparietal sulcus has been found to increase from childhood to adulthood (age 8–19), and these changes in activation are associated with improvements in visual spatial working memory (Klingberg, Forssberg, & Westerberg, 2002; Kwon, Reiss, & Menon, 2002). It is noteworthy that these fMRI studies of age-related changes in brain function involved in working memory show different directional changes in activation compared to studies of brain function during tasks of attentional and inhibitory control. Furthermore, whereas some studies suggest that children and adults recruit similar regions of the brain during tasks of visual spatial working memory (Klingberg et al., 2002; Kwon et al., 2002; Thomas et al., 1999), another study showed a developmental shift in the location of active voxels during performance (Scherf, Sweeney, & Luna, 2006; similar to the findings of Bunge et al., 2002). That is, children showed increased activation in the caudate nucleus, the thalamus and the anterior insula, whereas adolescents showed activation in the right dorsolateral prefrontal cortex, and adults showed concentrated activation in the left prefrontal and posterior parietal regions (Scherf et al., 2006). Behaviorally, children demonstrated poorer task performance compared to adolescents and adults, which may suggest that changes in location of activation may affect age-related performance differences.

Developmental changes have been found not only for working memory abilities critical to maintaining information online, but also for the ability to manipulate information in working memory. In one study, adults engaged the dorsolateral prefrontal cortex and superior parietal cortex when the task required participants to reverse the order of items held in working memory, whereas 8- to 12-year-old children did not engage this circuitry, and their performance on reversal trials suffered (Crone, Wendelken, Donohue, van Leijenhorst, & Bunge, 2006). Interestingly, children did recruit these frontal and parietal regions during encoding and response selection, but not during the delay period, when manipulation was required. These findings suggest that a brain region (e.g., prefrontal cortex) can exhibit adult-like patterns of activation in one task condition, but not in another.

Developmental changes in the structural and functional connections among a core memory neural circuit of hippocampus and MTL areas with prefrontal and parietal cortex have also been explored (Ghetti &

Bunge, 2012). Associated with the development of this functional brain network during middle childhood are improvements in several aspects of memory. One is the age-related improvement in recollection of specific episodes and of contextual details (Brainerd, Holliday, & Reyna, 2004; Ghetti & Angelini, 2008), which is accompanied by a developmental increase in prefrontal cortex fMRI activation elicited by memory encoding specifically associated with successful recollection (Ofen et al., 2007). Another is a developmentally related improvement in recollection of complex as compared to simpler scenes. Such scenes have been found to activate a network of regions including MTL cortex (parahippocampal gyrus) and prefrontal cortex. One study demonstrated that parahippocampal gyrus activity exhibited an age-related increase (disproportionate for high-complexity vs. low-complexity scenes), which predicted subsequent recollection (Chai, Ofen, Jacobs, & Gabrieli, 2010). Another developmental change in MTL concerns regional specificity within the hippocampus, a region of focus in this review. Specifically, age-related fMRI activity changes in the anterior region of the hippocampus have been found to be specifically related to increases in memory for associations critically supported by episodic or relational memory (Paz-Alonso, Ghetti, Donohue, Goodman, & Bunge, 2008; Ghetti, DeMaster, Yonelinas, & Bunge, 2010). Finally, one further developmental trend of note is the increase in strategic control of memory that is the use of more sophisticated strategies for effective monitoring and regulation of memory, as well as the use of better retrieval cues. This is related to development of effective connectivity of MTL memory areas with prefrontal and parietal cortices (Ghetti & Bunge, 2012). Moreover, the default mode functional brain network, which includes medial temporal cortex and prefrontal cortex, is said to be only sparsely functionally connected during childhood (ages 7–9 years) (Fair et al., 2008), but then integrates into a cohesive network in adulthood. Together, these age-related changes in memory function are helpful in understanding the development of various types of memory.

Whereas many of these investigations conclude that chronological age or maturation predicts the changes observed in activation patterns, critics raise the possibility that cognitive strategy, learning, or experience play a role in the results (Brown, Petersen, & Schlaggar, 2006; Dick, Leech, Moses, & Saccuman, 2006). For example, learning is speculated to parallel a shift toward increasingly sparse patterns of activation, such that the set of central neural resources involved in controlled and novice processing becomes less essential as skilled, automatic, and efficient processing emerges (Poldrack, 2010), a pattern that parallels some of the reported results of decreases in activation with age. The roles of plasticity and environmental enrichment (Greenough, Black, & Wallace, 1987), which includes physical activity, are also important factors to consider when making conclusions about developmental changes.

PHYSICAL ACTIVITY, AEROBIC FITNESS, AND THE BRAIN AND COGNITION

A growing number of studies demonstrate that participation in physical activity and individual differences in aerobic fitness positively influence cognition, brain structure, and brain function during childhood. The research is motivated by an established body of animal and human research that suggests that physical activity and aerobic exercise can positively influence cognition and the brain in rodents and older adults. Extending these findings to a child population has significance for the role of health behaviors in the biological potential of the developing brain during a critical period of maturation.

In younger and older rodents, voluntary wheel running has been found to lead to enhanced learning and retention (van Praag, Shubert, Zhao, & Gage, 2005), as well as improved structural integrity of the brain, via the growth of new neurons (van Praag, Christie, Sejnowski, & Gage, 1999; van Praag, Kempermann, & Gage, 1999) in the hippocampus and vasculature in many brain regions (Clark, Brzezinska, Puchalski, Krone, & Rhodes, 2009). Exercise has also led to increased production of neurotrophins, such as brain-derived neurotrophic factor (BDNF), involved in cell survival and synaptic plasticity (Cotman & Berchtold, 2002), and insulin-like growth factor (IGF-1), crucial for exercise-induced angiogenesis (Lopez-Lopez, LeRoith, & Torres-Aleman, 2004) and neurogenesis in the dentate gyrus of the hippocampus (Trejo, Carro, & Torres-Aleman, 2001). These results provide a basis for understanding molecular mechanisms involved in the structural and functional brain changes with physical activity and aerobic fitness in humans.

The majority of physical activity and exercise studies with humans have focused on older adults. This focus on the elderly is motivated by the question of whether the often-observed decline of cognition and brain function that accompanies aging can be slowed or reversed (at least temporarily) with physical activity. This research has, in general, tentatively provided a positive answer to this question. In elderly humans, fitness-training interventions have been shown to engender improvements in cognitive control and aspects of memory (Colcombe & Kramer, 2003; Erickson et al., 2009; Erickson et al., 2011; Heyn, Abreu, & Ottenbacher, 2004). The cognitive enhancements appear to be driven, in part, by increases in brain volume in frontal, parietal, and hippocampal regions (Colcombe et al., 2006; Erickson et al., 2011; Floel et al., 2010; Gordon et al., 2008; Ruscheweyh et al., 2011) and changes in fMRI activation and functional connectivity with physical activity and exercise (Colcombe et al., 2004; Voss et al., 2010). Indeed, the patterns of functional brain change exhibited by older adults who participated in aerobic exercise programs appear to become more similar to that exhibited by younger adults, compared to their less fit peers (Colcombe et al., 2004; Voss et al., 2010). Additionally, a randomized controlled trial demonstrated that 1 year of

aerobic exercise training was sufficient to increase the volume of the aging hippocampus, potentially reversing age-related volume loss (Erickson et al., 2011). Alternatively, older adults involved in a stretching and toning program for 1 year showed hippocampal atrophy, typical for the age group in the study (Erickson et al., 2011).

Together, the rodent and human research with the elderly has begun to provide insights into the neural basis for the effects of exercise on the human brain and cognition. This research also suggests that one might expect beneficial effects of physical activity and aerobic fitness on cognition and the brain in children. Thus far, the majority of accumulating evidence of the positive association among physical activity, aerobic fitness, cognition, and the brain in children mostly comes from cross-sectional studies; that is, studies that compare groups of high and low fit children. These studies provide a foundation for longitudinal randomized controlled trials to be conducted in children, which will allow researchers to make causal conclusions about the relationship of exercise and brain health in children that have been found in rodents and older adults.

Aerobic Fitness and Cognition in Children

In children, like older adults, aerobic fitness has been associated with cognitive control and memory in the laboratory. Higher fit 9- and 10-year-old children have been found to outperform lower fit children on flanker tasks (Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Hillman, Buck, Themanson, et al., 2009; Pontifex et al., 2011; Voss et al., 2011) and Stroop tasks (Buck et al., 2008), which tap aspects of attention and inhibition, as well as memory paradigms (Chaddock, Erickson, Prakash, Kim, et al., 2010; Chaddock et al., 2011). For example, during a flanker task, higher fit children were faster to respond to the direction of a central target amid distractors (e.g., >>>>>, >><>>), as well as more accurate on the task (Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Hillman, Buck, Themanson, et al., 2009; Pontifex et al., 2011). Performance differences are more evident during incongruent flanker trials (e.g., >><>>), which require increased inhibitory control, relative to congruent trials (e.g., >>>>>) (Chaddock, Erickson, Prakash, VanPatter, et al., 2010; Chaddock, Erickson, et al., 2012; Pontifex et al., 2011; Voss et al., 2011). However, global benefits of aerobic fitness across both congruent and incongruent flanker trials have also been shown (Hillman, Buck, Themanson, et al., 2009).

During memory tasks, higher fit children (age 9–10) have demonstrated better memory recognition performance when memory items were studied relationally (i.e., items studied as a pair or triplet) compared to non-relationally (i.e., items studied individually) (Chaddock, Erickson, Prakash, Kim, et al., 2010; Chaddock et al., 2011). In addition, children (age 7–10

years) placed into a physical activity group designed to improve aerobic fitness showed preferential viewing time to faces that had been paired with scenes during relational memory encoding after 9 months of activity, compared to children placed into a wait-list control group (Monti, Hillman, & Cohen, 2012). No group differences in eye movements were found for nonrelational memory trials, which supports the reported selective benefit of aerobic fitness on relational memory (Chaddock, Erickson, Prakash, Kim, et al., 2010; Chaddock et al., 2011). Together, the research suggests a positive association between aerobic fitness and cognition during childhood. To strengthen these findings, longitudinal randomized controlled interventions are needed to investigate how participation in physical activity and improvements in aerobic fitness influence specific elements of cognition during childhood.

Aerobic Fitness and Brain Structure in Children

Recent cross-sectional studies are the first to use MRI to investigate how these fitness differences in performance on tasks of cognitive control and memory relate to brain structure in 9- and 10-year-old children. The studies in children specifically focused on the basal ganglia and hippocampus, two regions that have been found to relate to exercise and aerobic fitness in rodents and older adults.

Basal Ganglia

In children, Chaddock, Erickson, Prakash, VanPatter, et al. (2010) observed that enhanced cognitive control associated with higher aerobic fitness related to differences in the volume of specific regions of the basal ganglia (Chaddock, Erickson, Prakash, VanPatter, et al., 2010). Relative to their lower fit peers, higher fit children (age 9–10) had increased inhibitory control during a flanker task, coupled with a larger dorsal striatum (Chaddock, Erickson, Prakash, VanPatter, et al., 2010). No relationship was found among fitness, task performance, and volume of the ventral striatum, a region with functions unrelated to cognitive control (Aron et al., 2009). The findings suggested that aerobic fitness differences in flanker task performance may relate to differences in the volume of specific regions of the basal ganglia (Chaddock, Erickson, Prakash, VanPatter, et al., 2010). In particular, the dorsal striatum, an important structure for cognitive control, motor integration, and response resolution (Aron et al., 2009), may be particularly sensitive to aerobic fitness in children. Further, the findings are supported by research in rodents, which has shown that voluntary wheel running led to increases in the production of brain-derived neurotrophic factor (Aguiar, Speck, Prediger, Kapczynski, & Pinho, 2008; Marais, Stein, & Daniels, 2009) and astrocytes (Li et al., 2005) in the dorsal striatum, as well as research in

older adults (Verstynen et al., 2012), which has shown that the volume of the caudate nucleus of the dorsal striatum mediated the relationship between aerobic fitness and cognitive performance on a task requiring mental flexibility (Verstynen et al., 2012).

Hippocampus

Volumes of other brain structures, such as the hippocampus, have also been found to relate to aerobic fitness in children, older adults, and rodents (Chaddock, Erickson, Prakash, Kim, et al., 2010; Cotman & Berchtold, 2002; Erickson et al., 2009; Erickson et al., 2011; Pereira et al., 2007). In one study, higher fit children (age 9–10) showed larger bilateral hippocampal volumes and superior relational memory performance compared to lower fit children, and bilateral hippocampal volume served to partially mediate the relationship between fitness and relational memory performance (Chaddock, Erickson, Prakash, Kim, et al., 2010). Furthermore, hippocampal volume was positively associated with performance on the relational but not the nonrelational memory task. These findings support rodent research, which has shown that wheel running led to increased cell proliferation and survival (van Praag, Christie, et al., 1999; van Praag, Kempermann, et al., 1999), vasculature (Clark et al., 2009), growth factors (Cotman & Berchtold, 2002), dendritic structure (Redila & Christie, 2006), gliogenesis (Uda, Ishido, Kami, & Masuhara, 2006) in the hippocampus, coupled with improved learning and memory (van Praag et al., 2005), as well as research in older adults, which has demonstrated that 1 year of aerobic exercise training was sufficient to increase the volume of the hippocampus, potentially reversing age-related volume loss (Erickson et al., 2011).

Aerobic Fitness and Brain Function in Children

Other studies have used measures of functional neuroimaging (e.g., event-related potentials [ERPs], functional magnetic resonance imaging [fMRI]) to examine the association between aerobic fitness and the brain across the lifespan.

Event-Related Potentials (ERPs)

ERPs are electrical recordings of the brain's activity, obtained from the scalp, that are linked to the occurrence of an event, such as the presentation of a stimulus or the execution of a response. To compute an ERP, a continuous electroencephalogram (EEG) is recorded by electrodes placed on the scalp during a cognitive task. Then, epochs of the recorded EEG are time-locked to the onset of a stimulus or the initiation of a response to a stimulus and averaged over a number of trials. As a result of averaging, variation between trials is removed, thereby revealing a characteristic ERP pattern of the brain's response. The resulting ERP is divided into components, characteristic

portions of the response that have been linked to specific psychological processes. Notably, the P3, a positive ERP component that occurs approximately between 300 and 800 ms following stimulus presentation, has been related to attention allocation during stimulus engagement. Further, the error-related negativity (ERN) is a response-locked ERP component that emerges following conflicting information or error production and is thought to represent cognitive control operations involved in action monitoring.

Physical activity and aerobic fitness influences on brain function, measured via ERPs, began with the study of older adults. Whereas such findings in the cognitive aging literature paved the way for the study of fitness effects on brain function during childhood, the findings have been reviewed in several other scholarly publications (e.g., Hillman, Buck, & Themanson, 2009; Kramer & Hillman, 2006), and hence will not be reviewed herein. More recently, several researchers (Hillman et al., 2005; Hillman, Buck, Themanson, et al., 2009; Pontifex et al., 2011) have investigated the P3 component of the stimulus-locked ERP and have shown that higher fit children had a larger mean amplitude and a shorter mean latency than lower fit children. Contemporary theory suggests that the P3 reflects neuronal activity associated with revision of the mental representation of the environment (Donchin, 1981). Its amplitude is governed by the allocation of attentional resources when working memory is updated (Donchin & Coles, 1988), such that P3 amplitude is sensitive to the amount of attentional resources allocated to a stimulus (Polich, 1987; Polich & Heine, 1996). P3 timing, marked by its peak latency, is thought to represent stimulus evaluation and classification speed (Duncan-Johnson, 1981; Ilan & Polich, 1999; Verleger, 1997). Thus, fitness-related findings have suggested that higher fit children allocate greater attentional resources and have faster cognitive processing speed relative to their lower fit peers (Hillman et al., 2005; Hillman, Buck, Themanson, et al., 2009), with additional research suggesting that higher fit children also exhibit greater flexibility in the allocation of attentional resources, as indexed by greater modulation of P3 amplitude across tasks that vary in the amount of cognitive control required for successful task completion (Pontifex et al., 2011). Since higher fit children have also demonstrated better performance on tasks of cognitive control, the P3 component appears to represent the effectiveness of a subset of cognitive processes that support willed action within the stimulus environment (Hillman, Buck, Themanson, et al., 2009; Pontifex et al., 2011).

In addition, several ERP studies (Hillman, Buck, Themanson, et al., 2009; Pontifex et al., 2011) have focused on aspects of cognition that entail the control or monitoring of one's actions. Specifically, the relation of fitness on cognitive control has been explored using the response locked ERN component. The ERN is observed in ERP averages that are commonly

elicited by errors of commission during task performance. It is believed to represent either the detection of errors during task performance (Gehring, Goss, Coles, Meyer, & Donchin, 1993; Holroyd & Coles, 2002) or more generally the detection of response conflict (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Yeung, Botvinick, & Cohen, 2004), which may be engendered by errors in response production. Several studies have reported that higher fit children exhibited smaller ERN amplitude during tasks which emphasized the speed of responding (Hillman, Buck, Themanson, et al., 2009), and more flexibility in the allocation of these resources during tasks requiring variable cognitive control demands, as evidenced by changes in ERN amplitude for higher fit children and a lack of modulation of ERN in lower fit children (Pontifex et al., 2011). Researchers have suggested a relationship between aerobic fitness and the efficient use of different cognitive control strategies.

Together, these findings provide evidence that children with lower levels of fitness allocate fewer attentional resources during stimulus engagement (i.e., smaller P3 amplitude) and exhibit delays in cognitive processing speed (i.e., longer P3 latency), but increase neural resources underlying the monitoring of their actions (i.e., larger ERN amplitude). Conversely, higher fit children allocate greater attentional resources during stimulus interaction within the environment and exhibit less reliance upon action monitoring processes: only increasing resource allocation (i.e., larger ERN amplitude) to meet the demands of more challenging task environments. Under more demanding task conditions, lower fit children's strategies appear less effective, as they perform more poorly under conditions requiring the upregulation of cognitive control.

Functional Magnetic Resonance Imaging (fMRI)

The P3 data raise the possibility that higher fit children are better at recruiting cognitive control networks (Gehring & Knight, 2000), and the ERN data further suggest that higher levels of fitness enhance the monitoring of conflict in the (dorsal) anterior cingulate cortex, a brain region that evaluates conflict (often engendered via errors), and signals the need to adjust cognitive control (Dosenbach et al., 2007). Two studies using blood oxygen level dependent (BOLD) fMRI in children (Chaddock, Erickson, et al., 2012; Voss et al., 2011) extend the ERP studies by gaining spatial sensitivity in detecting the regional locations and networks that are associated with higher aerobic fitness levels and superior task performance during childhood. That is, specific brain regions are suggested to play a role in the monitoring (anterior cingulate cortex) for alterations in attentional and interference control (middle and inferior frontal gyrus, precentral gyrus) in the presence of distractors and response conflict (superior parietal cortex), as well as the preparation and generation of a motor response (supplementary motor area; Banich et al., 2000). Voss et al. (2011) showed that higher fit and lower fit

children differed in fMRI activity in these regions associated with response execution and inhibition, task set maintenance, and top-down regulation. Behaviorally, higher fit children showed greater overall accuracy and less interference cost than lower fit children, yet the study examined brain activation in performance-matched higher fit and lower fit children to gain insight into different task strategies as a function of aerobic fitness level during childhood. When the trials on the flanker task were more difficult (i.e., during incongruent, relative to congruent, trials), lower fit children showed greater activation in the network of brain regions associated with cognitive control. The authors interpreted these data in terms of the influence of fitness on the efficient use of different cognitive control strategies.

Chaddock, Erickson, et al. (2012) also showed fitness differences in fMRI activity in these frontal and parietal regions during an event-related flanker task design (to extend Voss et al.'s [2011] block design). The study explored task performance and activation as a function of flanker task conditions that varied in cognitive control demands (e.g., congruent, incongruent) (Voss et al., 2011) as well as the time on task (first half of the task, second half of the task). Both higher fit and lower fit children showed increased recruitment of frontal and parietal regions during initial engagement with the congruent flanker condition, followed by a decrease in activity with additional performance. No within-group changes in congruent accuracy were observed across task blocks, despite a decline in performance across all participants, likely due to fatigue. However, during the incongruent flanker condition, only higher fit children maintained accuracy across blocks, coupled with increased prefrontal and parietal recruitment in the early task block and reduced activity in the later block. Lower fit children showed a decline in incongruent accuracy across blocks, and no changes in activation. These results provide additional support that aerobic fitness in children influences brain circuits involved in cognitive control (Hillman, Buck, Themanson, et al., 2009; Pontifex et al., 2011). Together, the ERP and fMRI studies of brain function in children suggest that aerobic fitness is involved in an ability to adapt neural processes to meet and maintain task goals.

PHYSICAL ACTIVITY INTERVENTIONS IN CHILDREN

There is a need to supplement cross-sectional studies with randomized, controlled trials in which children are placed into a physical activity intervention group and a control group. With a longitudinal design, cognition and/or brain function are examined before and after the intervention to establish a causal relation between changes in physical activity and aerobic fitness and cognitive and brain health. A randomized control trial is currently ongoing at the University of Illinois (i.e., the FITKids

trial), involving the current authors, with MRI, fMRI, DTI, ERP, and cognitive measures. Several recently reported intervention studies on the influence of physical activity on neurocognition during childhood have yielded promising results.

One intervention study extended cross-sectional research (Chaddock, Erickson, et al., 2012; Voss et al., 2011) by suggesting that physical activity during childhood may enhance specific elements of frontal brain function involved in cognitive control (Chaddock-Heyman et al., 2013). Specifically, 8- to 9-year-old children who participated in 60+ min of physical activity, 5 days per week for 9 months, showed decreases in fMRI brain activation in a region of the right anterior prefrontal cortex, coupled with within-group improvements in performance during incongruent flanker trials of increased cognitive control. Children assigned to a wait-list control group did not show changes in brain activation. Furthermore, at post-test, children in the physical activity group showed similar anterior frontal brain patterns and incongruent accuracy rates to a group of college-aged young adults (mean age of 22.5 years). Children in the wait-list control group still differed from the young adults in terms of anterior prefrontal activation and performance at post-test. These data raise the possibility that participation in physical activity during childhood may lead to more adult-like recruitment of prefrontal brain areas important for cognitive control.

In another longitudinal study (Davis et al., 2011) using fMRI, sedentary, overweight 7- to 11-year-old children were randomized to an exercise program for 13 weeks or to a non-exercise control condition (with no after school program). The treatment group played aerobic games (e.g., running games, jump rope, basketball, soccer) and either met for 20 min per day or 40 min per day. Only the high-dose aerobics group (40 min per day) showed increases in cognitive control (for the most demanding cognitive function measure, “planning,” as measured by the Cognitive Assessment System) and mathematics achievement. Increases in prefrontal cortex fMRI activity and decreases in parietal cortex fMRI activity were also found for the high dose physical activity intervention group during an antisaccade task of cognitive control, but performance on this task was not reported (Davis et al., 2011).

Additionally, Kamijo et al. (2011) used ERP techniques to investigate working memory (using a modified Sternberg task) before and after a 9-month physical activity intervention compared to a wait-list control group in children, ages 7–10. Improvements in task performance were found following the intervention during task conditions that placed larger demands upon working memory, relative to task conditions with smaller working memory demands. In addition, increased amplitude of the contingent negative variation (CNV), an ERP component reflecting cognitive and motor preparation, was observed at post-test over frontal scalp sites in the physical activity intervention group. No differences in performance or brain activation

were noted for the wait-list group. Such findings suggest that prolonged physical activity participation supports improvements in working memory and its neural underpinnings during tasks requiring more extensive amounts of cognitive control (Kamijo et al., 2011). These interventions provide a preliminary understanding of the influence of physical activity on the brain during childhood. Additional randomized controlled trials, which include broader measures of cognition and measures of brain structure and fMRI brain function at pre- and post-test, will be important in order to gain additional insight into the effects of physical activity on the cognitive and brain health of children.

Real-World Behavior

It is important to understand whether the benefits of aerobic fitness and physical activity extend outside the laboratory to everyday functions. In a real-world setting, participation in physical activity and higher levels of aerobic fitness have been associated with increased academic achievement (Castelli et al., 2007; Chomitz et al., 2009; Coe et al., 2006; Grissom, 2005; Roberts, Freed, & McCarthy, 2010; see Chapter 7). In addition, higher levels of fitness during childhood have been found to relate to higher performance on a real-world task of street crossing. In this study, a street intersection was modeled in a virtual environment, and higher and lower fit 8- to 10-year-old children navigated trafficked roads by walking on a manual treadmill that was integrated with an immersive virtual world (Chaddock, Neider, Lutz, Hillman, & Kramer, 2012). Child pedestrians crossed the street while undistracted, listening to music, or conversing on a hands-free cellular phone. Higher fit children maintained street crossing success rates across all three conditions, whereas lower fit children showed decreased success rates when on the hands-free phone, relative to the undistracted and music conditions. A lack of fitness group differences in physical measures of crossing speed suggests that multitask performance differences were not driven by differences in walking speed. Together, the results suggest that higher levels of childhood aerobic fitness may attenuate the impairment typically associated with multitasking during street crossing. It is possible that superior cognitive abilities of higher fit children play a role in the performance differences during complex real-world tasks. Additional research is needed to understand the transfer of fitness-related cognitive and neural benefits to everyday functions.

CONCLUSION

In sum, this review provides evidence for a positive relationship between physical activity, aerobic fitness, and the cognitive and brain health of

children. Physical activity and aerobic fitness have been found to benefit cognition and brain structure and function involved in attention, inhibition, and memory; skills important for scholastic achievement and daily living (Strong et al., 2005). The results have implications for the biological potential of the brain during periods of maturation and brain development, and suggest that the developing brain is plastic and sensitive to lifestyle factors. This research is also important because children are becoming increasingly sedentary and unfit, with increased risk for disease (CDC, 2009; USDHHS, 2008). This review raises the possibility that physical activity and aerobic fitness can enhance the cognitive health of the developing brain during childhood, a critical period of maturation.

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