A functional MRI investigation of the association between childhood aerobic fitness and neurocognitive control[☆]

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ABSTRACT

We used functional magnetic resonance imaging (fMRI) to examine brain activity of higher fit and lower fit children during early and late task blocks of a cognitive control flanker paradigm. For congruent trials, all children showed increased recruitment of frontal and parietal regions during the early block when the task was unfamiliar, followed by a decrease in activity in the later block. No within-group changes in congruent accuracy were reported across task blocks, despite a decline in performance across all participants, likely due to fatigue. During incongruent trials, 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. We suggest that higher fit children are better at activating and adapting neural processes involved in cognitive control to meet and maintain task goals.

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1. Introduction

Research has shown a relationship between aerobic fitness, brain, and cognition across the lifespan. Although the majority of studies linking aerobic activity and fitness to neurocognitive improvements involve older adults (Colcombe and Kramer, 2003; Colcombe et al., 2004, 2006; Etnier et al., 2006; Heyn et al., 2004; Kramer et al., 1999), a growing literature illustrates that higher levels of aerobic fitness also relate to higher academic achievement, superior cognitive abilities, larger brain structures, and elevated brain function in children (Castelli et al., 2007; Chaddock et al., 2010a,b, 2011; Chomitz et al., 2009; Davis et al., 2011; Hillman et al., 2009; Pontifex et al., 2011; Sibley and Etnier, 2003). Despite these

reports, educational systems often de-emphasize the importance of physical activity during the school day.

In the present study, we used functional magnetic resonance imaging (fMRI) to examine the association between aerobic fitness and brain function in children. Specifically, we focused on differences in brain activity of higher fit and lower fit children during a cognitive control task. Cognitive control (also known as "executive control") refers to a set of higher order processes associated with the control of thought and action (Botvinick et al., 2001; Meyer and Kieras, 1997; Norman and Shallice, 1986). Higher levels of cognitive control permit the selective focus of attention, inhibition of inappropriate or interfering responses, flexible thinking, and maintenance of information in working memory. These abilities have been shown to relate to academic attainment in mathematics and reading (Bull and Scerif, 2001; DeStefano and LeFevre, 2004; St. Clair-Thompson and Gathercole, 2006).

Higher levels of aerobic fitness have been associated with superior cognitive control in children (Chaddock et al., 2010b; Hillman et al., 2009; Kamijo et al., 2011; Pontifex et al., 2011) and across the lifespan (Colcombe and Kramer, 2003; Etnier et al., 2006; Smith et al., 2010). Specifically, higher fit children outperform their lower fit peers on tasks of cognitive control (Chaddock et al., 2010b; Hillman et al., 2009) and show a superior ability to upregulate control processes to meet increased task demands (Chaddock et al.,

submitted for publication; Pontifex et al., 2011). These performance differences have been associated with neural differences such that higher fit and lower fit children differ in event-related brain potential (ERP) indices (Hillman et al., 2009; Kamijo et al., 2011; Pontifex et al., 2011) and basal ganglia volumes (Chaddock et al., 2010b).

In this study, we employed fMRI to examine aerobic fitness-related differences in the functional neural circuitry underlying cognitive control during development. By using fMRI we gain spatial sensitivity over previous ERP studies in detecting the regional locations and networks that are associated with higher aerobic fitness levels. Brain activity of higher fit and lower fit children was recorded during the administration of a modified Eriksen flanker paradigm, a cognitive control task of conflict resolution in which participants were required to attend to a centrally presented stimulus amid laterally presented flanking stimuli (Eriksen and Eriksen, 1974; Kramer et al., 1994). We focused on the cortical circuitry involved in responding to congruent (e.g., < < < < <) and incongruent (e.g., < < > < <) flanker trials, where the incongruent condition requires greater attentional and interference control to filter potentially misleading flankers that are mapped to incorrect behavioral responses.

Neuroimaging studies of cognitive control across the lifespan have identified regions of the prefrontal and parietal cortices involved in selective spatial attention and the resolution of response conflict (Botvinick et al., 1999; Bunge et al., 2002; Casey et al., 2000; Colcombe et al., 2004; Hazeltine et al., 2000). For example, 8- to 12-year-old children with high performance on a flanker/go-no-go task of interference suppression and response resolution showed activation in the left prefrontal cortex and bilateral parietal cortex (Bunge et al., 2002). In an elderly population, prefrontal and parietal activation (i.e., middle frontal gyrus, superior frontal gyrus, anterior cingulate cortex, superior parietal cortex) has been reported during the performance of an arrow flanker task (Colcombe et al., 2004). Of particular interest to the present study, fitter older participants showed different activation patterns in these brain regions, coupled with higher task performance, relative to lower fit individuals (Colcombe et al., 2004).

Given the established positive association between aerobic fitness, brain and cognition across the lifespan (Colcombe et al., 2004; Hillman et al., 2008), it is likely that aerobic fitness is associated with the neural circuitry supporting cognitive control during development. Thus, we hypothesized that higher fit and lower fit children would show differences in fMRI signal in the attentional neural network coupled with differences in performance on the flanker task.

Furthermore, to extend the literature on fitness and cognitive control, we examined the relation between childhood aerobic fitness, flanker task performance and fMRI activation patterns during time on task (i.e., at different points in task performance). Some neuroimaging studies have examined adult brain plasticity as a function of learning, practice, and performance early and late in an experimental session, and results range from decreases in activation, increases in activation, to shifts in active brain regions across time (Chein and Schneider, 2005; Landau et al., 2004; Milham et al., 2003; Nyberg et al., 2003; Olesen et al., 2003; Poldrack et al., 1998; Tracy et al., 2001). We reasoned that, if aerobic fitness supports the capacity to learn, adapt, and/or withstand fatigue, the dynamics of brain activity involved in cognitive control may vary as a function of fitness level. To test these hypotheses, we examined brain activity during the early and late task blocks of the flanker paradigm in a preadolescent population of higher fit and lower fit children. To the extent that fitness may engender higher levels of cognitive control, one might expect that higher fit children would display better performance, and differential patterns of brain activation,

Table 1
Participant mean demographic and fitness data (*SD*) by aerobic fitness group.

Variable	Lower fit	Higher fit
N	18(7 boys)	14 (9 boys)
Age (years)	10.1 (0.5)	9.7 (0.6)
VO$_2$ max (mL/kg/min)	36.6 (4.4)[*]	53.1 (4.5)[*]
VO$_2$ max Percentile (%)	14.2 (17.7)[*]	83.3 (5.0)[*]
K-BIT[a] Composite Score (IQ)	115.6 (16.1)	115.1 (7.7)
K-BIT[a] Crystallized Score (Vocabulary)	110.1 (11.0)	109.5 (7.8)
K-BIT[a] Fluid Score (Matrices)	117.6 (18.7)	117.6 (10.1)
ADHD[b]	5.5 (3.7)	7.6 (4.7)
Tanner[c]	1.7 (0.5)	1.5 (0.5)
SES[d] (median)	2.8 (0.5)	2.9 (0.4)

[*] Significantly different at $p < 0.001$.
[a] Kaufman Brief Intelligence Test (Kaufman and Kaufman, 1990).
[b] Scores on the *ADHD Rating Scale V* (DuPaul et al., 1998).
[c] Pubertal timing assessed using a modified Tanner Staging System (Tanner, 1962; Taylor et al., 2001).
[d] Socioeconomic status. SES was determined by the creation of a trichotomous index based on three variables: child participation in a free or reduced-price lunch program at school, the highest level of education obtained by the child's mother and father, and the number of parents who worked full-time (Birnbaum et al., 2002).

with increasing fatigue, particularly in the most challenging task conditions.

2. Method

2.1. Participants

Preadolescent 9- and 10-year-old children were recruited from East-Central Illinois. Children were screened for several factors that influence physical activity participation or cognitive function. To begin, the Kaufman Brief Intelligence Test (K-BIT; Kaufman and Kaufman, 1990) was administered to each child to obtain a composite intelligence quotient (IQ) score including both crystallized and fluid intelligence measures. Participants were excluded if their scores were more than 1 standard deviation below the mean (85%). Next, a guardian of the child completed the Attention-Deficit Hyperactivity Disorder (ADHD) Rating Scale IV (DuPaul et al., 1998) to screen for the presence of attentional disorders. Participants were excluded if they scored above the 85th percentile. Pubertal timing was also assessed using a modified Tanner Staging System (Tanner, 1962; Taylor et al., 2001) with all included prepubescent participants at or below a score of 2 on a 5-point scale of developmental stages. In addition, socioeconomic status (SES) was determined by creating a trichotomous index based on three variables: participation in a free or reduced-price meal program at school, the highest level of education obtained by the child's mother and father, and the number of parents who worked full-time (Birnbaum et al., 2002).

Furthermore, eligible participants were required to (1) qualify as higher fit or lower fit (see Section 2.2), (2) demonstrate right handedness (as measured by the Edinburgh Handedness Questionnaire; Oldfield, 1971), (3) report no adverse health conditions, physical incapacities, or neurological disorders, (4) report no use of medications that influenced central nervous system function, (5) successfully complete a mock MRI session to screen for claustrophobia in an MRI machine, (6) sign an informed assent approved by the University of Illinois at Urbana-Champaign, and (7) show less than 2 mm of motion during the fMRI paradigm. A legal guardian also provided written informed consent in accordance with the Institutional Review Board of the University of Illinois at Urbana-Champaign.

Thirty-two children were included in the analysis, including 14 higher fit participants (9 boys, 5 girls) and 18 lower fit participants (7 boys, 11 girls). No statistically reliable differences in age, gender, socioeconomic status or Kaufman Brief Intelligence Test (KBIT) scores existed between aerobic fitness groups. Table 1 provides a list of demographic and fitness information for the final sample.

2.2. Aerobic Fitness Assessment

The aerobic fitness level of each child was determined at the first visit by measuring maximal oxygen uptake (VO$_2$ max) using a computerized indirect calorimetry system (ParvoMedics True Max 2400) during a modified Balke protocol (American College of Sports Medicine, 2006). Specifically, participants ran on a motor-driven treadmill at a constant speed with increases in grade increments of 2.5% every 2 min until volitional exhaustion. Averages for oxygen uptake (VO$_2$) and respiratory exchange ratio (RER) (the ratio between carbon dioxide and oxygen) were assessed every 30 s. In addition, heart rate was measured throughout the fitness test (using a Polar heart rate monitor [Polar WearLink®+ 31, Polar Electro, Finland]), and ratings of perceived exertion were assessed every 2 min using the children's OMNI scale (Utter et al., 2002).

VO$_2$ max was defined when oxygen consumption remained at a steady state despite an increase in workload. Relative peak oxygen consumption 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 greater than 185 beats per minute (American College of Sports Medicine, 2006) accompanied by a heart rate plateau (i.e., an increase in work rate without a concomitant increase in heart rate, Freedson and Goodman, 1993), (3) RER greater than 1.0 (Bar-Or, 1983), and/or (4) ratings on the children's OMNI scale of perceived exertion greater than 8 (Utter et al., 2002). Relative peak oxygen consumption was expressed in mL/kg/min.

Aerobic fitness group assignments (i.e., higher fit and lower fit) were based on whether a child's VO_2 max value fell above the 70th percentile or below the 30th percentile according to normative data provided by Shvartz and Reibold (1990). Children who did not qualify as higher fit or lower fit were excluded from further participation. All participants were compensated $20 for participation.

2.3. Imaging method

Higher fit and lower fit children completed a series of structural and functional MRI scans. Prior to scanning, all participants were tested for visual acuity, and corrective lenses were added to MRI safe plastic frames to ensure a corrected vision of at least 20/40 while in the scanner. The lenses and frames did not obstruct a mirror above participants' eyes that enabled them to view images on a back projection.

Structural MRI protocol. High-resolution T1-weighted brain images were acquired using a 3D MPRAGE (Magnetization Prepared Rapid Gradient Echo Imaging) protocol with 144 contiguous axial slices, collected in ascending fashion parallel to the anterior and posterior commissures, echo time (TE) = 3.87 ms, repetition time (TR) = 1800 ms, field of view (FOV) = 256 mm, acquisition matrix 192 mm × 192 mm, slice thickness = 1.3 mm, and flip angle = 8°. All images were collected on a 3T head-only Siemens Allegra MRI scanner.

Functional MRI protocol. Functional MRI scans were acquired during an event-related modified Eriksen flanker task (Eriksen and Eriksen, 1974). The task required individuals to respond as quickly as possible to the direction of a central arrow in an array of arrows presented on an MRI back projection. A congruent trial consisted of > > > > > and < < < < < arrow displays in which the target arrow was flanked by arrows of the same direction. An incongruent trial consisted of > > < > > and < < > < < arrow displays in which the target arrow was flanked by the opposing arrow response. Trials in which the middle arrow pointed to the right (e.g., > > > > >, < < > < <) required a right index finger button press (via a MRI compatible response box), while trials in which the middle arrow pointed to the left (e.g., < < < < <, > > < > >) required a left index finger button press.

During the task, 20 trials of each of the four possible arrow presentations (> > > > >, < < < < <, < < > < <, > > < > >) were presented in a random order. Each array of arrows was presented for 1500 ms, and each stimulus array was separated by a fixation cross (+) presented for 1500 ms. Forty additional fixation crosses that jittered between 1500 ms and 6000 ms were also randomly presented after the constant 1500 ms fixation cross throughout the task. The jitter prevented participants from expecting a specific frequency of responding and was optimized for the timing and temporal resolution of the expected hemodynamic responses. White arrows and white fixation crosses were presented on a black background. The participant was engaged in the task for about 6 min, in addition to a 1 min block of 20 practice trials (five of each arrow arrays, presented randomly). Analysis was conducted on the first 3 min of the task ("early task block") (0–195 s) and the second 3 min of the task ("late task block") (196–360 s). Stimulus presentation, timing, and task performance measures were controlled by E-Prime software.

For the fMRI protocol during the flanker task, a fast echo-planar imaging (EPI) sequence with Blood Oxygenation Level Dependent (BOLD) contrast was employed. A total of 247 volumes (TR = 1500 ms; TE = 25 ms; flip angle = 80°) were collected for each subject.

2.4. Image analysis

Neuroimaging data analysis was conducted using FSL 4.1.5 (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). Preprocessing of the functional data included motion correction via a rigid body algorithm in MCFLIRT (Jenkinson et al., 2002), removal of non-brain structures using BET (Brain Extraction Technique; Smith et al., 2002), spatial smoothing using a 5.0 mm FWHM (full width at half maximum) three-dimensional Gaussian kernel, and temporal filtering with a high pass frequency cut-off of 100 s. All children showed less than 1.88 mm of motion in all volumes (after excluding 6 higher fit children and 6 lower fit children who showed excessive motion), and the extent of motion did not differ between higher fit and lower fit children. In addition, the high-resolution T1 structural images of each participant were skull-stripped using BET (Smith et al., 2002).

The pre-processed functional images of each child were spatially registered to their individual skull-stripped high-resolution anatomical image, and then to a study-specific template in stereotaxic space. Registrations were conducted using a 12-parameter affine transformation (FMRIB's Linear Image Registration Tool (FLIRT); Jenkinson and Smith, 2001; Jenkinson et al., 2002). The study-specific template was created by warping each participant's high-resolution scan to MNI space via FLIRT, creating an average of these registered images, and spatially smoothing the average image with an 8 mm FWHM Gaussian kernel. We employed a template for registration in an effort to minimize the amount of warping during the registration

Table 2

Local maxima coordinates (Talairach coordinates; MNI space) of 18 mm (diameter) peak ROIs, derived from group localized clusters showing activation to both congruent and incongruent conditions across the flanker task.

	Peak Z statistic	x (mm)	y (mm)	z (mm)
Left middle frontal gyrus	5.75	−30	−10	58
Right middle frontal gyrus	5.55	36	−6	60
Supplementary motor area	8.97	−8	0	50
Anterior cingulate cortex	6.36	6	6	44
Left superior parietal cortex	7.36	−30	−48	42
Right superior parietal cortex	7.18	32	−52	38

process, to protect against registration bias, and to avoid registration complications by registering children's brains to an adult standard template.

Following pre-processing and registration, regression-based analysis of each participant's fMRI data was carried out using FSL's FEAT Version 5.98 (Beckmann et al., 2003). The time series at each voxel was modeled against the expected time series model derived by convolving the onset of each event type (congruent and incongruent flanker trials) with a double-gamma function, representing the expected time course of the hemodynamic response function. Only correct flanker trials were included in the model, and error trials were entered as covariates of no interest. Note that the same high pass temporal filtering applied to the data was applied to the general linear model (GLM) for the best possible match between the data and model. In addition, the temporal derivative was entered into the model (i.e., shifting the waveform slightly in time) to achieve a better model fit to the data and to reduce unexplained noise.

The first level analysis calculated a parameter estimate for the fMRI model at each voxel to estimate how strongly the model waveform fit the data, and this analysis resulted in voxel-wise statistical parametric maps for the entire brain of each individual for the congruent and incongruent conditions, and for comparisons and conjunctions between congruent and incongruent trials. Specifically, given our interest in differences in activation during the early and late blocks of the task, we modeled the first 3 min of the task (volumes 0–131, 0–195 s) and the second 3 min of the task (volumes 132–247, 196–360 s) separately. This separation allowed us to examine both the main effects of the task and aerobic fitness as well as how fitness moderated brain dynamics across different blocks of the paradigm.

Next, the individual brains were forwarded to a higher level mixed-effects group analysis to find areas across participants that were sensitive to congruent and incongruent trials. Higher level group analyses were carried out using FLAME (FMRIB's Local Analysis of Mixed Effects). To ensure that individual and group differences in gray matter volume did not confound the results, estimated total mean gray matter volume for each subject, smoothed with 4 mm HWHM kernel, was used as a voxel-wise covariate in the higher level FLAME analyses. All results from the final whole-head analyses resulted in Z statistic images that were thresholded by $Z > 2.33$ and a (corrected) cluster significance threshold of $p < 0.05$ (Worsley, 2001).

The group analysis helped to localize areas of the cortex that were sensitive to congruent and incongruent trials across the task and across all participants. These clusters showing activation to both congruent and incongruent flanker trials (i.e., conjunction) relative to the fixation baseline were determined using the above thresholds, and 18 mm (diameter) masks around cluster peaks (which contained 257 voxels, 2056 mm³) were used as functionally defined regions of interest (ROIs) from which mean percent signal change (versus baseline) was extracted for both the congruent and incongruent flanker conditions. It is important to note that the location and extraction of these clusters were done independently of any effects associated with aerobic fitness. Therefore, the localization of these clusters was unbiased in relation to our predictor variables. Specifically, six regions of interest, left middle frontal gyrus (LMFG), right middle frontal gyrus (RMFG), supplementary motor area (SMA), anterior cingulate cortex (ACC), left superior parietal lobule (LSPL), and right superior parietal lobule (RSPL) (see Fig. 1) were examined to explore the hypothesis that aerobic fitness in developing children can impact the neural network activated during the flanker paradigm (Colcombe et al., 2004). The peak of each region of interest was chosen by determining the x, y, and z coordinates with the highest z value within the region as labeled by the Harvard-Oxford Cortical and Subcortical Structural Atlases) (Harvard Center for Morphometric Analysis, http://www.fmrib.ox.ac.uk/fsl/data/atlas-descriptions.html) (see Table 2).

2.5. Statistical analysis

Differences in flanker task performance and fMRI mean percent signal change as a function of aerobic fitness group, congruency, and task block were explored via omnibus multivariate repeated measures, 2 (higher fit, lower fit) × 2 (congruent, incongruent) × 2 (early task block, late task block) ANOVAs. If the omnibus ANOVA reached significance, post hoc comparisons were performed (with Bonferroni-corrected t tests). The family-wise alpha level was set at $p = .05$.
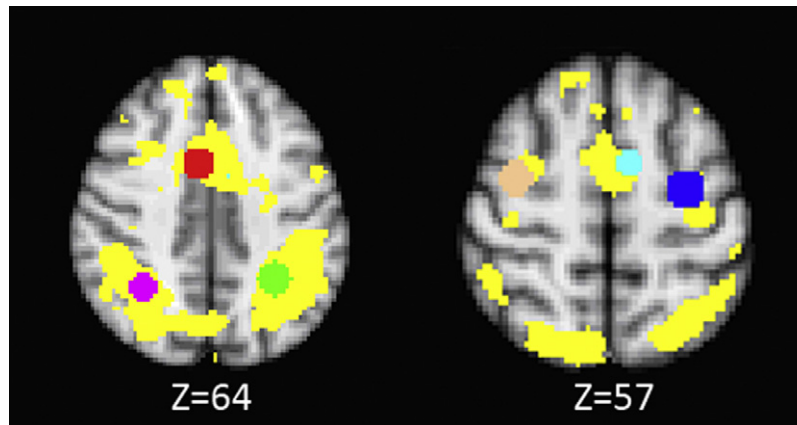
Fig. 1. Areas shown in yellow indicate clusters active during both congruent and incongruent flanker trials relative to baseline, across all participants, during the early and late task blocks. The 18 mm (in diameter) spheres (2056 mm^3) show the ROIs created based on the peaks within these clusters (see Table 2). LMFG = dark blue; RMFG = copper; SMA = light blue; ACC = red; LSPL = green; RSPL = purple. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

3. Results

3.1. Task performance

Accuracy. There was a significant main effect of task block ($F(1, 30) = 9.2$, $p = 0.005$), such that the accuracy decreased from the early task block to the late task block, across both aerobic fitness groups and both task conditions. The fitness × condition × task block interaction was marginally significant ($F(1, 30) = 2.1$, $p = 0.1$), suggesting that changes in accuracy across the experiment varied as a function of both aerobic fitness group and task condition. Although this effect was not significant, given our *a priori* hypotheses, we explored this trend by conducting separate repeated measures 2 (higher fit, lower fit) × 2 (early task block, late task block) ANOVAs for congruent and incongruent flanker trials. A main effect showed a decrease in congruent accuracy independent of fitness group from

the early task block to the late task block ($F(1, 30) = 5.4$, $p = 0.03$). No interaction with fitness was found ($F < 0.4$, $p > 0.5$). Exploratory paired *t*-tests within each fitness group showed that changes in congruent accuracy across task blocks was not significant for either the higher fit (t < 1.6, p > 0.1) or lower fit (t < 2, p > 0.05) groups (see Fig. 2 and Table 3). A main effect also showed a decrease in incongruent accuracy independent of fitness group from the early task block to the late task block ($F(1, 30) = 10.5$, $p = 0.003$). Further, an interaction ($F(1, 30) = 4.1$, $p = 0.05$) demonstrated that higher fit participants maintained their accuracy on incongruent trials across both task blocks ($t(13) = 1.7$, $p > 0.05$), while lower fit participants showed decreased performance during the late task block relative to the early task block ($t(17) = 3.2$, $p = 0.006$) (see Fig. 2 and Table 3).

Reaction time. There was a main effect of condition ($F(1, 30) = 21.8$), with longer RTs during incongruent trials ($M = 814$ ms; $SE = 19$ ms) compared to congruent trials ($M = 767$ ms; $SE = 17$ ms),
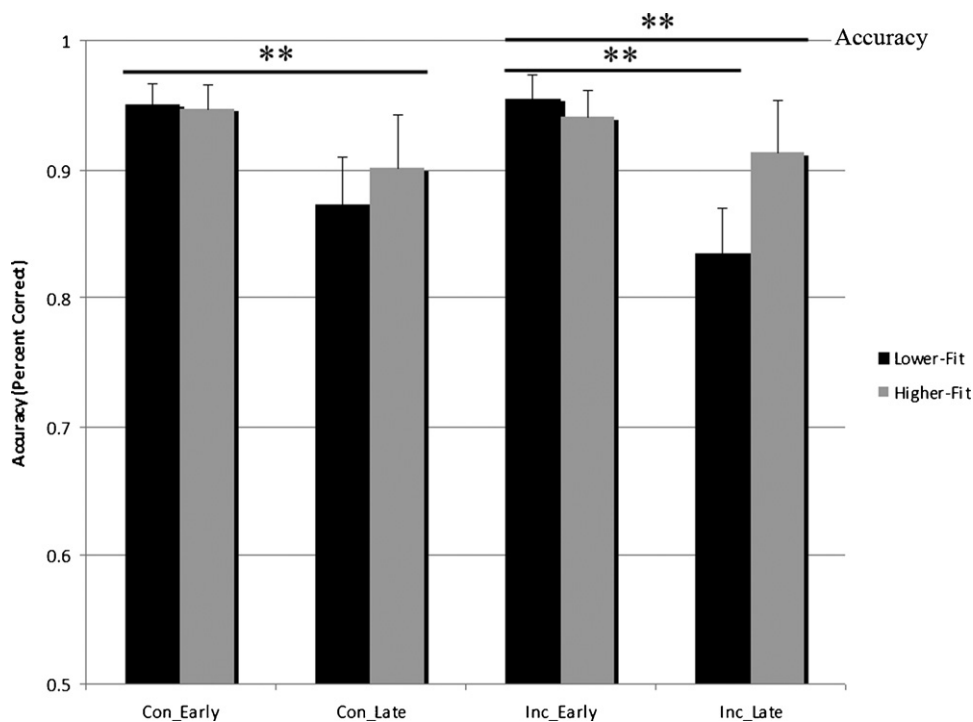

Fig. 2. Flanker task accuracy by congruency and aerobic fitness group, during the early and late blocks of the flanker task.

Table 3
Task performance (SD) (i.e., accuracy and reaction time) by aerobic fitness group during the early flanker task block and late flanker task block.

Test	Lower fit		Higher fit	
	Early	Late	Early	Late
Congruent accuracy (%)	95.0 (6.9)	87.2 (17.2)	94.7 (7.1)	90.1 (13.0)
Incongruent accuracy (%)	95.5 (5.4)	83.4 (17.6)	94.1 (10.0)	91.3 (12.1)
Congruent reaction time (ms)	740.4 (107.1)	782.9 (125.0)	760.5 (48.0)	785.8 (86.5)
Incongruent reaction time (ms)	784.7 (120.8)	856.2 (140.2)	780.0 (71.6)	834.3 (99.3)

and a main effect of time (F (1, 30) = 25.8), with longer RTs during the late task block (M = 815 ms; SE = 20 ms) relative to the early task block (M = 766 ms; SE = 16 ms). No fitness effects or interactions were found for RT (all $p > 0.9$) (see Table 3).

3.2. fMRI

Left middle frontal gyrus (LMFG). A main effect of task block indicated that mean percent signal change in the LMFG decreased from the early to late task blocks, across all participants, and across both task conditions (F (1, 30) = 22.9, $p < 0.0001$). A fitness × condition × task block interaction (F (1, 30) = 5.7, $p = 0.02$) was decomposed with separate 2 (higher fit, lower fit) × 2 (early, late) ANOVAs for congruent and incongruent trials. For congruent trials, a main effect indicated that all participants had a significant decrease in mean percent signal change during the late task block compared to the early task block (F (1, 30) = 14.1, $p = 0.001$). No interaction with fitness was found (F (1, 30) = 0.76, $p = 0.39$) (see Fig. 3). For incongruent trials, a main effect demonstrated a significant decrease in mean percent signal change during the late task block relative to the early task block (F (1, 30) = 14.1, $p = 0.001$). An interaction (F (1, 30) = 5.7, $p = 0.024$) indicated that higher fit children showed less activation during the late task block (M = 0.05; SD = 0.31) relative to the early task block (M = 0.41; SD = 0.35) (t (13) = 4.6, $p = 0.001$) for incongruent trials, whereas lower fit children did not show significant changes in incongruent activation across the task blocks (t (13) = 1.9, $p = 0.08$). Higher fit children also showed a trend for greater activation during incongruent trials

relative to lower fit children during the early task block (t (30) = 1.9, $p = 0.06$) (see Fig. 3).

Right middle frontal gyrus (RMFG). A main effect of condition (F (1, 30) = 7.9, $p = 0.009$) demonstrated greater mean percent signal change in the RMFG during incongruent trials compared to congruent trials. A fitness × task block interaction (F (1, 30) = 9.3, $p = 0.005$) demonstrated that, across both congruent and incongruent trials, lower fit children showed a significant increase in RMFG signal change from the early task block (M = 0.11; SE = 0.14) to the late task block (M = 0.47; SE = 0.16) (t (17) = 2.5, $p = 0.02$), while higher fit children showed a less prominent decrease in activation between the early task block (M = 0.61; SE = 0.16) and the late task block (M = 0.24; SE = 0.18), which only reached marginal significance (t (13) = 1.9, $p = 0.08$). Higher fit children also showed greater activation than lower fit children during the early task block only for incongruent trials (t (30) = 2.7, $p = 0.01$) (see Fig. 3).

Supplementary motor area (SMA). The omnibus results of the SMA paralleled the results of the LMFG, with a main effect of task block (F (1, 30) = 11.8, $p = 0.002$) and a fitness × condition × task block interaction (F (1, 30) = 5.8, $p = 0.02$). Specifically, a main effect for congruent trials (F (1, 30) = 8.3, $p = 0.007$) indicated that all participants showed a significant decrease in mean percent signal change from the early task block (M = 0.33; SE = 0.05) to the late task block (M = 0.16; SE = 0.04) (see Fig. 3). For incongruent trials, a main effect (F (1, 30) = 8.1, $p = 0.008$) showed that all participants had less activation during the late task block relative to the early task block. A fitness × condition interaction (F (1, 30) = 5.2, $p = 0.03$) was also observed, and follow-up analyses indicated that higher fit children had less activation during the late task block (M = 0.15; SD = 0.18)
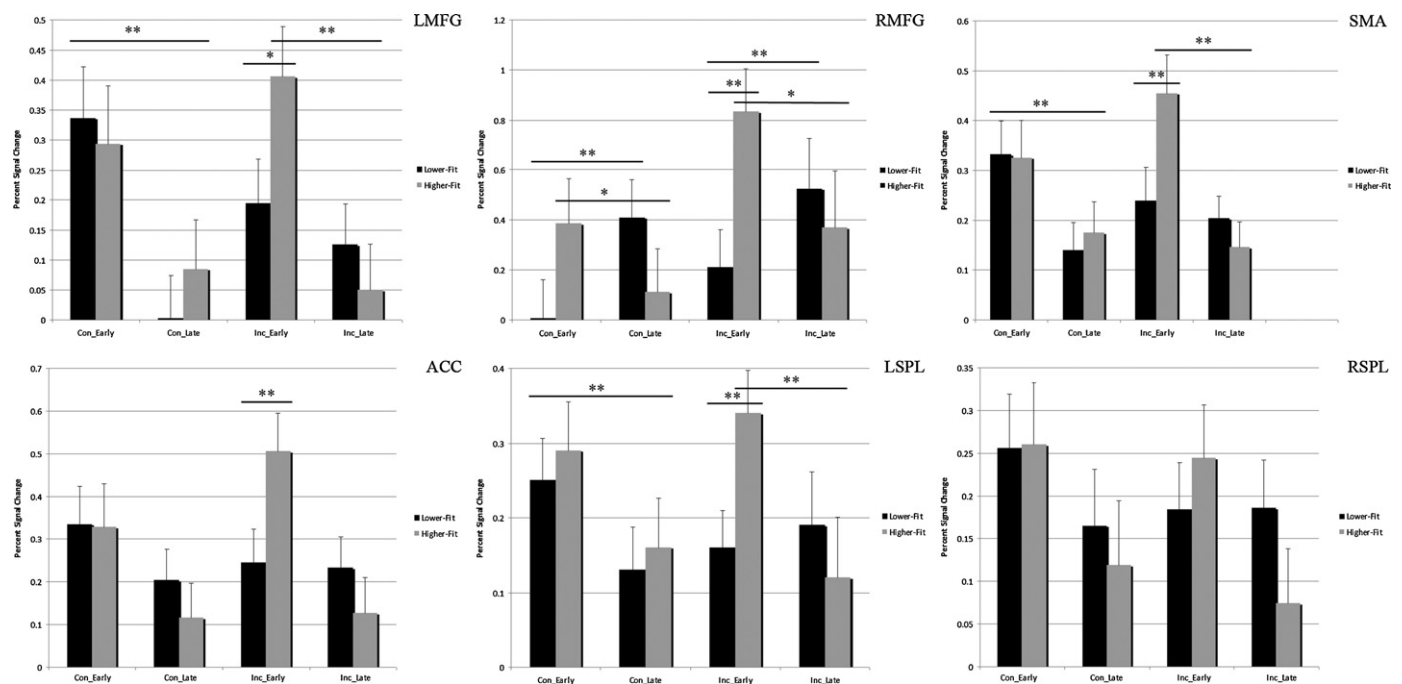

Fig. 3. Mean percent signal change for each ROI by congruency and aerobic fitness group, during the early and late blocks of the flanker task. $^*p < 0.09$; $^{**}p < 0.05$.

relative to the early task block ($M = 0.46$; $SD = 0.15$) (t (13) = 2.9, $p = 0.01$). Lower fit children did not show a change in mean percent signal change during incongruent trials across the task ($t < 0.6$, $p > 0.6$). In addition, higher fit children showed greater activation than lower fit children during the early task block for incongruent trials (t (30) = 2.1, $p = 0.05$) (see Fig. 3).

Anterior cingulate cortex (ACC). A main effect of task block (F (1, 30) = 7.4, $p = 0.01$) showed less activation in the late task block ($M = 0.17$; $SD = 0.05$) compared to the early task block ($M = 0.35$; $SD = 0.06$). The fitness × condition × task block interaction was marginally significant (F (1, 30) = 3.3, $p = 0.08$), with the direction of the congruent and incongruent means following those of the LMFG and SMA. Higher fit children also showed greater activation than lower fit children during the early task block for incongruent trials (t (30) = 2.1, $p = 0.05$) (see Fig. 3).

Left superior parietal lobe (LSPL). The omnibus results of the LSPL paralleled the results of the LMFG and SMA, with a main effect of task block (F (1, 30) = 5.1, $p = 0.03$) and a fitness × condition × task block interaction (F (1, 30) = 4.7, $p = 0.04$). Specifically, a main effect was observed for congruent trials such that all children showed a decrease in congruent activation from early to late task blocks (F (1, 30) = 5.2, $p = 0.03$). No fitness × condition interaction was found ($F < 1$, $p > 0.9$) (see Fig. 3). For incongruent trials, a fitness × condition interaction (F (1, 30) = 4.7, $p = 0.04$) indicated that higher fit children showed less activation during the late task block ($M = 0.12$; $SD = 0.23$) relative to the early task block ($M = 0.34$; $SD = 0.27$) (t (13) = 2.8, $p = 0.01$), while lower fit children did not show changes in activation across the task blocks ($t < 0.4$, $p > 0.7$). In addition, higher fit children ($M = 0.34$; $SD = 0.27$) had more activation than lower fit children ($M = 0.16$; $SD = 0.16$) during the early task block for incongruent trials (t (13) = 2.3, $p = 0.03$) (see Fig. 3).

Right superior parietal lobe (RSPL). The omnibus ANOVA did not reach significance, but the direction of the means in the fitness × condition × task block interaction ($F = 0.7$, $p = 0.4$) matched that of the previously described regions (see Fig. 3).

Correlations between task performance and fMRI activation were not significant after correction for multiple comparisons.

4. Discussion

Aerobically fit children have been found to exhibit superior cognitive control relative to lower fit children, and performance differences are related to brain volumes and ERP indices thought to implement cognitive control (Chaddock et al., 2010b; Hillman et al., 2005, 2009; Kamijo et al., 2011; Pontifex et al., 2011). In this study, we extended previous investigations by using fMRI to determine whether higher fit and lower fit children showed different brain activation patterns and performance during an event-related flanker task. This was indeed the case. Further, the aerobic fitness differences in the brain and performance measures varied as a function of task difficulty and task block. In general, we suggest that aerobic fitness in children relates to the modulation of brain circuits involved in cognitive control.

Functional MRI brain activation measured during the flanker paradigm help provide a neural substrate for differences in performance as a function of aerobic fitness. During the congruent condition, all children, regardless of aerobic fitness level, had greater activation in the prefrontal and parietal cortex (i.e., LMFG, SMA, ACC, LSPL) early in task performance, followed by a significant reduction in activity in these regions later in the task. The fMRI patterns were coupled with no within-group changes in congruent accuracy across task blocks, despite a general decrease in accuracy across all participants. When increased cognitive demands were required during the incongruent condition, higher fit children showed greater activation than lower fit children in the prefrontal

and parietal cortex (i.e., LMFG, RMFG, SMA, ACC, LSPL) during the early task block, and only higher fit children demonstrated a decrease in brain activity in these regions across time, while maintaining a high level of accuracy. Lower fit children, on the other hand, demonstrated a decrease in accuracy on incongruent trials between the first and second halves of the task block, coupled with no change in fMRI activity in most regions of the attentional network. This pattern of results suggests that changes in brain activity across a flanker task vary as a function of childhood aerobic fitness and cognitive control demands.

The implementation of cognitive control in the brain involves the modulation of neural activity in accord with task demands (Banich, 2009). Increased brain activation can be interpreted to reflect an increase in resources devoted to the task, while less activity reflects a reduction in resources towards the task (Banich, 2009). Based on this framework, our results suggest that when task demands were low during congruent trials, both higher fit and lower fit children showed increased recruitment of prefrontal and parietal areas in the early task block when the task was unfamiliar, and then showed diminished resource allocation in the later block of the paradigm as the task became more familiar. However, accuracy for the congruent condition decreased across all participants (although accuracy was still quite high, even later in the block), suggesting that fatigue might have contributed to a reduction in resource allocation and decreased brain activity. Because overall task accuracy declined across all participants, we interpret the results in terms of fatigue rather than efficiency, learning, or practice.

When cognitive demands increased during the incongruent flanker condition, only higher fit children showed increased recruitment of prefrontal and parietal areas early in task performance, followed by a reduction in the magnitude of brain activity later in task performance. These changes in brain function were accompanied by the maintenance of performance across the experiment. Lower fit children did not demonstrate the same level of flexibility during the task as higher fit children. That is, activation in lower fit children during incongruent trials did not change across time, and task performance suffered. It is possible that increased recruitment in higher fit children during the early task block may have served to offset some of the fatigue effects later in the block. Our results parallel our previous reports indicating that aerobic fitness shows a stronger association to tasks that require more extensive amounts of cognitive control (i.e., incongruent trials) (Chaddock et al., 2010b, submitted for publication; Pontifex et al., 2011). However, as for congruent trials, both aerobic fitness groups may have diminished the allocation of neural resources towards the task, given that incongruent performance across all participants declined from the early to the late task block.

Together, the results suggest fitness-related differences in the adaptation of brain circuits related to cognitive control, in the face of growing fatigue. We specifically examined a network of prefrontal and parietal regions linked to attentional and interference control, key functions for successful performance of a flanker task (Banich et al., 2000; Botvinick et al., 1999; Bunge et al., 2002; Casey et al., 2000; Colcombe et al., 2004; Hazeltine et al., 2000). The dorsolateral prefrontal cortex, which includes the LMFG and RMFG, is said to play an important role in top-down attentional control and response inhibition. Specifically, these regions may be involved in the establishment of an attentional set for the selection, maintenance and manipulation of task-relevant information within working memory (Banich et al., 2000; Hazeltine et al., 2000; Liddle et al., 2001; Olesen et al., 2006). It is possible that increased activation in RMFG for lower fit children from early to late in the paradigm relates to a search for an alternative, compensatory strategy to increase attention and memory resources when unable to maintain task accuracy (see Cabeza, 2002; Colcombe et al., 2005 for similar

framework in older adults). Because left prefrontal activity has been shown to reflect high levels of cognitive control during childhood and right prefrontal activity is associated with high performance during adulthood (Bunge et al., 2002), it is possible that increased recruitment of the RMFG would not be beneficial in children.

Our results also support a role of the parietal cortex in cognitive control (Brass et al., 2005; Miller and Cohen, 2001; Tomita et al., 1999). Parietal areas are thought to be implicated in selective spatial attention (Corbetta et al., 2002; de Fockert et al., 2004; Mayer et al., 2004), maintenance of information (Banich et al., 2000; Corbetta et al., 2002; Jha and McCarthy, 2000; Jonides et al., 1993; Pollmann and von Cramon, 2000), and manipulation of items in working memory (Crone and Ridderinkhof, 2011; Olesen et al., 2003), all functions important for flanker task performance. In addition, some hypothesize that task-irrelevant and distractor representations are processed in parietal areas (Hazeltine et al., 2000) and regions of the prefrontal-parietal loop work to resolve the response competition and mismatch between task-relevant and task-irrelevant responses. Specifically, the ACC is said to be involved in the monitoring of response conflict (Banich et al., 2000; Hazeltine et al., 2000), which highlights its role in performance during attentional control (Liddle et al., 2001). Finally, a motor response to each flanker trial is likely generated in circuits involving the SMA (Nachev et al., 2008).

We suggest that childhood aerobic fitness is associated with the recruitment of these neural resources, which relates to the effectiveness of adapting to task demands and fatigue. The fMRI findings support and extend ERP research about childhood fitness and brain function by characterizing the functioning of the developing brain. In particular, the P3 and error-related negativity (ERN) ERP components are said to reflect cognitive control and attentional allocation as well as conflict monitoring and error evaluation, functions that involve the prefrontal cortex. Higher fit children have been shown to flexibly modulate the P3 and ERN to meet more difficult flanker task demands, which relates to higher response accuracy, while a failure to modulate the neuroelectric indices is accompanied by lower response accuracy in lower fit children (Hillman et al., 2009; Pontifex et al., 2011). Our results also suggest that higher fit children modulate cognitive control resources more flexibly than their less fit peers, and the current findings pinpoint specific brain regions that may be involved in the monitoring (ACC) for increased or decreased attentional and interference control (LMFG, RMFG) in the presence of distractors and response conflict (LSPL) as well as the preparation and generation of a motor response (SMA). Together, the neuroimaging studies suggest that childhood aerobic fitness is involved in an ability to adapt neural processes to meet and maintain task goals.

Our work also parallels aerobic fitness differences in brain activation and flanker task performance in an elderly population. Increased aerobic fitness in older adults has been found to relate to increased right prefrontal cortex activity and decreased ACC activation, coupled with improved conflict resolution (Colcombe et al., 2004). In the present study, we suggest that activation patterns of specific prefrontal and ACC regions increase and decrease in sync, which correspond to performance differences in higher fit and lower fit children across early and late stages of the task. As both decreased ACC activity (Colcombe et al., 2004) and increased ACC activity (Carlson et al., 2009) have been found to relate to increased task performance, additional studies are needed to explore the modulation of neural activity in the attentional network as a function of task performance and aerobic fitness. Connectivity among regions of interest should also be investigated. For example, in one study (Vallesi et al., 2009), a network of functionally connected regions including the left lateral prefrontal cortex, SMA and left SPL, is said to play a role in criterion-setting, which is defined as the capacity to employ relevant response criteria and suppress task-irrelevant distractors. Our complementary data raise the possibility that lower fit children show deficits in the neural network involved in criterion-setting.

Moreover, future research should aim to model the independent contributions of structural (e.g., Chaddock et al., 2010a,b) and functional plasticity in relation to childhood aerobic fitness and task performance to understand development more comprehensively. Correlations between task performance and fMRI activation would also add insight into fitness and neurocognitive development. Understanding test–retest reliability of BOLD fMRI effects (Bennett and Miller, 2010) in children (e.g., Koolschijn et al., 2011) would help to validate our results. It would also be interesting to examine whether reliability of fMRI signal differs as a function of childhood aerobic fitness group.

While our investigation provides a first step in understanding the relationship between childhood aerobic fitness and brain function as measured with fMRI, the cross-sectional design raises the possibility that the observed differences in performance and brain activation in higher fit and lower fit children were caused by another factor (e.g., genes, motivation, personality characteristics, nutrition, intellectual stimulation). Randomized, controlled interventions are needed to make causal conclusions about aerobic fitness and brain function during development. Furthermore, it is important for future research to study the mechanisms by which aerobic fitness may enhance brain function in children. Animal models have shown that aerobic exercise improves the structural integrity of rodent brains, via the growth and formation of new neurons, blood vessels and synapses (Cotman and Berchtold, 2002), as well as increases the production of neurochemicals (e.g., brain-derived neurotrophic factor, insulin-like growth factor) that promote the growth, survival and repair of brain cells (for review, see Voss et al., 2011). These changes are coupled with improved learning and memory (Gomez-Pinilla et al., 2008). The extent to which these mechanisms account for the benefits of aerobic fitness on neurocognitive control in humans deserves future exploration.

In conclusion, the present study provides new insight into the functional neurocognitive benefits of aerobic fitness during childhood. We suggest that higher fit children have a superior ability to activate frontal and parietal brain regions important for the monitoring, maintenance, and strategizing of higher level cognitive control abilities, important skills for academic performance in the classroom (Bull and Scerif, 2001; DeStefano and LeFevre, 2004; St. Clair-Thompson and Gathercole, 2006). The results provide additional evidence for the importance of a physically active lifestyle, aimed at improving aerobic fitness, during childhood.

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