FROM COGNITIVE MOTOR PREPARATION TO VISUAL PROCESSING: THE BENEFITS OF CHILDHOOD FITNESS TO BRAIN HEALTH

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Abstract—The association between a fit body and a fit brain in children has led to a rise of behavioral and neuroscientific research. Yet, the relation of cardiorespiratory fitness on premotor neurocognitive preparation with early visual processing has received little attention. Here, 41 healthy, lower and higher fit preadolescent children were administered a modified version of the Eriksen flanker task while electroencephalography (EEG) and behavioral measures were recorded. Event-related potentials (ERPs) locked to the stimulus onset with an earlier than usual baseline (-900/ -800 ms) allowed investigation of both the usual post-stimulus (i.e., the P1, N1 and P2) as well as the pre-stimulus ERP components, such as the Bereitschaftspotential (BP) and the prefrontal negativity (pN component). At the behavioral level, aerobic fitness was associated response accuracy, with higher fit children being more accurate than lower fit children. Fitness-related differences selectively emerged at prefrontal brain regions during response preparation, with larger pN amplitude for higher than lower fit children, and at early perceptual stages after stimulus onset, with larger P1 and N1 amplitudes in higher relative to lower fit children. Collectively, the results suggest that the benefits of being aerobically fit appear at the stage of cognitive preparation prior to stimulus presentation and the behavioral response during the performance of a task that challenges cognitive control. Further, it is likely that enhanced activity in prefrontal brain areas may improve cognitive control of visuomotor tasks, allowing for stronger proactive inhibition and larger early allocation of selective attention resources on relevant external stimuli. © 2015 IBRO. Published by Elsevier Ltd. All rights reserved.

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INTRODUCTION

Interest in physical activity as a health behavior to improve or maintain brain health first emerged in the aging literature, where a large body of literature exists (Colcombe et al., 2004; Hillman et al., 2008; Erickson et al., 2013), whereas physical activity and cognition research in preadolescent children is still in the early stages. Several studies have consistently shown that children with higher cardiovascular or aerobic fitness[†] have better academic achievement (see Keeley and Fox, 2009; Fedewa and Ahn, 2011 for reviews) and perform better on tasks tapping aspects of cognitive control and memory (Buck et al., 2008; Chaddock et al., 2011; Wu et al., 2011; Raine et al., 2013; Crova et al., 2014). In the last decade, a neuroscientific line of research has flourished, highlighting the impact of fitness-enhancing physical exercise (Davis et al., 2011; Hillman et al., 2014; Krafft et al., 2014) and exercise-related fitness (Hillman et al., 2009; Pontifex et al., 2009; Kamijo et al., 2010) on children's brain function and health (see Ahn and Fedewa, 2011; Chaddock et al., 2010, 2011: Hillman et al., 2011 for reviews) that also generalizes to special populations as overweight children (Davis et al., 2011; Krafft et al., 2014). The present work investigates aerobic fitness-related effects on the neural correlates of cognitive control in preadolescent children during a modified flanker task, which modulates cognitive control requirements through manipulation of interference control and response inhibition parameters. To this aim, we used event-related potentials (ERPs), which directly measure the electrical responses of the cortex to sensory, cognitive or motor events with a high temporal resolution.

Accordingly, Hillman and colleagues (2005) observed that in a stimulus discrimination (i.e., oddball) task, higher fit preadolescent children had larger amplitude of the P3-ERP component and better task performance than lower fit children. The P3 is a positive component occurring between 300 and 800 ms after stimulus onset over central-parietal brain areas, whose amplitude is related to the allocation of attentional resources during stimulus engagement, and its latency is associated with stimulus classification and evaluation and processing speed (Verleger et al., 2005; Polich, 2007). In subsequent studies, the authors (Hillman et al., 2009, 2014; Pontifex et al., 2011) confirmed that higher fit children had larger P3

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Abbreviations: ANOVA, analysis of variance; CNV, contingent negative variation; EEG, electroencephalography; EOG, electrooculography; ERN, error-related negativity; ERPs, event-related potentials; BP, Bereitschaftspotential; pN, prefrontal negativity; pP, prefrontal positivity.

 $^{^{\}dagger}$ The term "fitness" refers to aerobic or cardiovascular fitness throughout the manuscript.

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amplitude and were more accurate than their lower fit counterparts during a modified flanker task. These results indicated that performance accuracy is sensitive to individual differences in children's fitness, and that more efficient cognitive control subtends this behavioral outcome of fitness. Childhood fitness effects have also been observed in response-locked ERPs, showing more flexible attention toward errors and higher performance accuracy in higher compared to lower fit children (Hillman et al., 2009; Pontifex et al., 2011).

Pontifex et al. (2011) manipulated cognitive load of the flanker task through the inclusion of compatible and incompatible stimulus-response conditions. They found larger P3 and smaller error-related negativity (ERN) amplitude in high-fit than low-fit children, as well as a greater modulation of P3 and ERN between compatible and incompatible conditions, that were paralleled by higher accuracy especially under the incompatible condition. The authors interpreted the results in support of the dual mechanism of cognitive control theory proposed by Braver et al. (2007), postulating that cognitive control during working memory tasks operates via two strategies: proactive control (i.e., anticipatory process over the duration of a given task) and reactive control (i.e., transient process after stimulus perception). To interpret their fitness-related finding, Pontifex et al. (2011) proposed that higher fit children had greater reliance on the proactive control strategy, because they were able to flexibly upregulate their control across conditions, while maintaining stable response accuracy. On the contrary, lower fit children seemed to rely on a more reactive control strategy, because they presented difficulties in both the up-regulation required to process increased task demands and the flexible modulation required by the proactive control. Together, these results suggest that aerobic fitness may modulate task strategy, fostering the allocation of attentional resources during stimulus engagement and reducing the resource load devoted to action monitoring, which was associated with a more successful task performance through an efficient proactive control strategy. Another research has examined the contingent negative variation (CNV), which is a negative slow wave elicited during the interval between warning (S1) and imperative (S2) stimuli associated with the cognitive preparatory process during stimulus anticipation. A fitness-related enhancement of the CNV has been observed in children (Kamijo et al., 2011), adolescents (Stroth et al., 2009), and young adults (Kamijo et al., 2010), whereas fitness effects on brain function of preadolescent children during the pre-stimulus response preparation and early poststimulus ERP periods have not been investigated yet.

Recently, studies conducted with young and older adults (Berchicci et al., 2012, 2013, 2014; Perri et al., 2014a,b) have distinguished the contribution of two main components during the preparation of a motor response during visuo-motor discrimination tasks: the Bereitschaftspotential (BP) over medial central sites, which is a slow-rising negativity beginning more than 1 s prior to movement onset and reflecting motor preparation, and the prefrontal negativity (pN), maximal over prefrontal sites, which is a negative component beginning immediately prior to the BP and reflecting cognitive preparation of the response. Following stimulus onset, another large positive component - peaking between 200 and 300 ms over the prefrontal cortex - known as the prefrontal positivity (pP) has been proposed to reflect the stimulus-response mapping processing. In a recent study combining ERP and functional magnetic resonance imaging (fMRI) measures (Di Russo et al., 2013), the origin of pN was localized in the inferior frontal avrus within the prefrontal cortex, and this activity was associated with proactive control during response inhibition processes and predicted stimulus onset. Further, the pP was localized in the anterior insula, whose activity may represent the accumulation of evidences needed to complete the final stage of the decision-making process that leads to overt responding. The BP origin has been localized in the supplementary motor area and in the cinculated motor area (Shibasaki and Hallett, 2006; Di Russo et al., 2013). Nevertheless, the contribution of the prefrontal cortex during cognitive-motor control in preadolescents is still scarcely understood.

Critical questions remain regarding (1) how functional maturation in preadolescence is manifested during both motor and cognitive anticipatory processes (BP and pN components) and early perceptual processing (pP, P1, N1 and P2 components) in the preparation–perception–action cycle, and (2) how these processes and their behavioral outcomes are modulated by aerobic fitness. We hypothesized to find aerobic fitness-related changes in early visual processing, because of the specific fitness-related improvements in visual discrimination abilities, visual-search skills and visual concentration to environmental demands (Zwierko et al., 2014).

EXPERIMENTAL PROCEDURES

Participants

Forty-one healthy preadolescent children (mean ± SD: 10.0 ± 0.6 years of age: 23 female) were recruited for this study. Participants were classified as lower fit (N = 20) and higher fit (N = 21) on the basis of whether their VO₂max fell above the 70th percentile or below the 30th percentile, according to normative data provided by Shvartz and Reibold (1990), which apply to most of the industrial world. Thus, the adjective "fit" that identifies the groups specifically refers to aerobic or cardiovascular fitness. All participants were right handed (Edinburgh Handedness Inventory; Oldfield, 1971). The participants were free of neurological diseases, attentional disorders and physical disabilities, and had normal or corrected-to-normal vision, as reported by the participants' guardians. Legal guardians provided written informed consent and participants provided written informed assent in accordance with the Institutional review Board of the University of Illinois at Urbana-Champaign.

Task

Participants completed a modified version of the Eriksen flanker task (Eriksen and Eriksen, 1974). The stimuli were 3-cm tall white arrows constituting a 16.5-cm wide array

with a vertical visual angle of 1.32° and a horizontal visual angle of 7.26°, which were presented focally for 200 ms on a black background with a fixed inter-stimulus interval of 1700 ms. Participants were instructed to make a left or right button press depending on the direction of a centrally presented arrow amid either congruous (e.g., < < < < or >>>>>) or incongruous (e.g., <<><< or >><>>) flanking arrows (Hillman et al., 2006; Pontifex and Hillman, 2007). The incongruent, relative to the congruent, condition necessitates the concurrent activation of both the correct response (elicited by the target) and the incorrect response (elicited by the flanking stimuli) before stimulus evaluation is complete, thus requiring greater amounts of interference control to inhibit the flanking stimuli and execute the correct response (Spencer and Coles, 1999). In the compatible stimulus-response condition, participants pressed the button as quickly and accurately as possible corresponding to the same direction in which the central arrow pointed. Following completion of the compatible condition, participants then completed an incompatible stimulus-response condition, wherein participants were instructed to respond as quickly and accurately as possible in the direction opposite to that of the centrally presented target arrow (Friedman et al., 2009). This condition manipulates task difficulty through multiple levels of conflict (i.e., perceptual and response conflict) such that the incongruent incompatible condition requires the greatest amount of control to manage response conflict and inhibitory processing. For each compatibility condition, two blocks of 100 trials were presented with equi-probable congruency and directionality. Response time and response accuracy were collected as behavioral measures.

Electroencephalography (EEG) recording and analysis

EEG activity was recorded from 64 electrode sites arranged in an extended montage based on the International 10–10 System (Chatrian et al., 1985) using a Neuroscan Quik-Cap (Compumedics, Charlotte, NC, USA). Recordings were re-referenced to averaged mastoids (M1, M2), with AFz serving as the ground electrode, and impedance at less than 10 k Ω . Additional electrodes were placed above and below the left orbit and on the outer canthus of each eye to monitor electrooculography (EOG) activity with a bipolar recording. Continuous data were digitized at a sampling rate of 500 Hz, amplified 500 times with a DC to 70-Hz filter, and a 60-Hz notch filter using a Neuroscan Synamps 2 amplifier. Continuous data were processed off-line to reduce EOG artifacts using the Gratton et al. (1983) algorithm.

To comprehensively examine the brain activity related to both response preparation and stimulus perception, EEG recordings were separately segmented and averaged into non-overlapping 1800-ms epochs that were measured from 900 ms before to 900 ms after the stimulus onset. The segmentation and further analyses were separately performed for compatible and incompatible stimulus–response conditions, collapsed across congruency, because a preliminary sample-bysample *t*-test did not show significant differences (all ps > 0.5).

Raw EEG data were visually inspected to identify and discard epochs contaminated with artifacts prior to signal averaging. The first trial of each block was discarded from further analysis. The trials with amplitude exceeding threshold of $\pm 120 \,\mu V$ were automatically excluded from the averaging. To further reduce high-frequency noise. the time-locked EEG grand-averages were band-pass filtered using an IIR filter (0.01-25 Hz; 24 dB/oct). The baseline was derived from the mean amplitude over the initial 100 ms of the averaged epochs. This approach allows investigating not only the post-stimulus ERP components [i.e., pP. P1. N1, and P2], but also the prestimulus components related to the movement preparation [i.e., BP and pN], since the baseline was calculated from 900 to -800 ms before the stimulus onset and not immediately prior to the stimulus onset, as typically done for the examination of later ERP components such as the N2 and P3.

The mean amplitude in the -600/0-ms time window, reflecting activity during the pre-stimulus preparation stage, was selected for further analysis on the following electrodes: Cz (roughly overlaying pre-motor and motor areas) for the BP component; Fpz (over the prefrontal cortex) for the pN component (Di Russo et al., 2013). After stimulus onset, the change in amplitude (i.e., delta) between the negative peak immediately after stimulus onset and the subsequent positive peak over the prefrontal site (Fpz) was taken as measure of the pP. Peak amplitudes and latencies of the post-stimulus ERP components were calculated with the typical baseline (-100)0 ms) for each participant in the following time windows: P1: 80-150 ms, N1: 130-200 ms, and P2: 180-300 ms. The electrode selection was based on both the scalp topography, which allowed identification of the greatest activity for a given component at the group level (i.e., the P1, N1 and P2 on PO7 or PO8), and previous reports (e.g., Shibasaki and Hallett, 2006; Berchicci et al., 2012). Later components, such as the N2 and the P3, were not considered in this study because they were the focus of a previous publication from the same dataset (Pontifex et al., 2011).

To visualize the voltage topography of the ERP components, spline interpolated 3-D maps were constructed using the BESA 2000 software (MEGIS Software GmbH, Gräfelfing, Germany).

Statistical analysis

All statistical analyses were conducted using a significance level of p = .05 (Statistica v.10; StatSoft). Task performance (mean RT, response accuracy) was analyzed separately using a 2 (Aerobic fitness: higher fit, lower fit) × 2 (Compatibility: compatible, incompatible) repeated measures analysis of variance (ANOVA). Post hoc comparisons were performed using Bonferroni corrections; effect size was calculated using partial eta squared (η^2). The BP and pN mean amplitude and the pP delta amplitude were submitted to a 2 (Aerobic fitness: higher fit, lower fit) × 2 (Compatibility: compatible, incompatible) repeated measures ANOVA on the Cz and Fpz electrode,

respectively. The P1. N1 and P2 components were assessed separately for amplitude and latency using a $2 \times 2 \times 2$ ANOVA with aerobic fitness (higher fit, lower fit) as group factor, and Compatibility (compatible, incompatible) and Sites (PO7, PO8) as repeated measures. Post hoc comparisons were performed using Bonferroni corrections; effect size was calculated using partial eta squared (n^2) . Given a sample size of 41 participants and beta of .20 (i.e., 80% power), the present research design theoretically had sufficient sensitivity to detect repeated measures aerobic effects exceeding f = 0.388 and Aerobic fitness fitness \times Compatibility interactions exceeding f = 0.224(assuming correlation between repeated measures ≥ 0.5). For t-test differences, the present design theoretically had sufficient sensitivity to detect effects exceeding d = 0.897(with a two-sided alpha) as computed using G*Power 3.1.2 (Faul et al., 2007).

RESULTS

Behavioral results

The mean response times and accuracy for each group are presented in Table 1. The repeated-measures ANOVA revealed neither a main effect for aerobic fitness, nor a significant Aerobic fitness × Compatibility interaction ($F_{1,39} = 3.3$, p = 0.08, $\eta^2 = 0.06$) for RT. However, there was a main effect for aerobic fitness on accuracy ($F_{1,39} = 10.0$, p = 0.002, $\eta^2 = 0.21$), with higher fit children being more accurate than lower fit children, and a significant Aerobic fitness × Compatibility interaction ($F_{1,39} = 6.7$, p = 0.01, $\eta^2 = 0.15$). Post hoc analysis revealed a significant difference between compatible and incompatible conditions for the lower fit group (p = 0.02) and between higher and lower fit groups in the incompatible condition (p = 0.001).

Electrophysiological results

Fig. 1 shows the grand averaged ERP waveforms at the representative prefrontal (Fpz), central (Cz), and parietal-occipital (PO8) sites, where the considered components were maximal. Before stimulus onset, a slow-rising negativity (pN) over the prefrontal regions was detectable and modulated by both aerobic fitness and compatibility. Indeed, the amplitude of the pN is larger in higher than lower fit children, and in the incompatible relative to the compatible condition. At the medial central site (Cz), the BP is also present, showing a slow-rising negativity that reflects motor readiness or preparation. The BP component looks similar regardless of aerobic fitness group or compatibility condition. After stimulus onset, another large component over the

prefrontal cortex is detectable: the pP, whose delta amplitude (from the previous negative peak to the actual prefrontal positive peak) is not modulated by compatibility or aerobic fitness. Over parietal-occipital sites, the typical visual components of the ERPs, such as the P1, N1 and P2, can be observed with a voltage baseline in the typical early pre-stimulus period (from 200 to 0 ms). With respect to the P1 component, differences in amplitude can be observed as a function of aerobic fitness, whereas the differences in amplitude of the N1 and the P2 as a function of the considered variables are less pronounced.

Statistical analysis of the pN mean amplitude showed a main effect for aerobic fitness ($F_{1.39} = 4.4$, p = 0.04, $\eta^2 = 0.10$), with larger pN amplitude in higher $(-7.0 \pm 1.5 \,\mu\text{V})$ compared to lower fit $(-2.6 \pm 1.5 \,\mu\text{V})$ children, and for compatibility ($F_{1,39} = 5.9$, p = 0.02, $\eta^2 = 0.13$), with larger amplitude in the incompatible $(-5.5 \pm 1.1 \,\mu\text{V})$ compared to the compatible $(-4.0 \pm 1.1 \,\mu\text{V})$ condition. The ANOVA did not reveal a significant Aerobic fitness × Compatibility interaction $(F_{1,39} = 2.5, p = 0.1, \eta^2 = 0.06)$. Statistical analysis of the BP mean amplitude did not yield significant results as a function of Aerobic fitness ($F_{1,39} = 0.08$, p = 0.8, $\eta^2 = 0.001$), or Compatibility ($F_{1,39} = 1.3$, p = 0.3, $\eta^2 = 0.03$), or their interaction ($F_{1,39} = 1.3$, p = 0.3, $\eta^2 = 0.03$). Analysis of the delta pP amplitude did not indicate a main effect or interaction (all ps > 0.3).

While the analysis on the P1 latency did not indicate a significant effect, P1 amplitude indicated a main effect for Aerobic fitness ($F_{1,39} = 4.3$, p = 0.04, $\eta^2 = 0.09$), with larger amplitude for higher ($13.8 \pm 1.5 \,\mu$ V) compared to lower fit ($9.4 \pm 1.5 \,\mu$ V) children. The P1 amplitude was affected by site ($F_{1,39} = 7.8$, p = 0.007, $\eta^2 = 0.16$), with larger amplitude for PO8 ($12.8 \pm 1.1 \,\mu$ V) than PO7 ($10.3 \pm 1.1 \,\mu$ V).

Analysis of the N1 latency did not yield significant results. Although the N1 peak amplitude was not affected by Aerobic fitness ($F_{1.39} = 0.3$, p = 0.6, d = 0.X), it was affected by Compatibility ($F_{1.39} = 5.3$, p = 0.03, $\eta^2 = 0.12$), with larger amplitude in the incompatible $(-3.8 \pm 1.0 \,\mu\text{V})$ compared to the compatible $(-2.6 \pm 1.0 \,\mu\text{V})$ condition. Further, the interaction of Aerobic fitness \times Condition \times Site was significant ($F_{1,39} = 4.4$, p = 0.04, $\eta^2 = 0.10$). In particular, Bonferroni post hoc analysis revealed larger N1 amplitude at the PO8 (mean amplitude $-3.8 \pm 1.3 \,\mu\text{V}$) relative to the PO7 (mean amplitude $-2.6 \pm 0.8 \,\mu\text{V}$) site in both compatible and incompatible conditions for both higher fit (p = 0.005 and p < 0.001, respectively) and lower fit (p = 0.017 and p < 0.001. respectively) children.

Analysis of P2 latency and amplitude did not yield significant results (all ps > 0.35).

 Table 1. Mean and standard error (SE) of the response time (ms) and response accuracy (percent correct responses) as a function of Fitness and Compatibility

	Lower fit		Higher fit	
	Compatible condition	Incompatible condition	Compatible condition	Incompatible condition
RT (mean ± SE) Accuracy (mean ± SE)	532.0 ± 23.0 79.9 ± 1.8	567.0 ± 30.0 73.6 ± 2.6	523.0 ± 22.0 85.2 ± 1.7	512.0 ± 29.0 86.0 ± 2.5



Fig. 1. Grand average ERP waveforms at the prefrontal (Fpz), central (Cz) and parietal-occipital (PO8) sites. Time zero represents the stimulus appearance. Waveforms of the groups as a function of Fitness and Compatibility are superimposed and identified by black/red color (Fitness) and solid/dotted line (Compatibility). The main components are labeled in the figure. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Topographical maps

Three-dimensional topographical maps are displayed in Fig. 2. The maps in the top row show the negative activity over the prefrontal cortex in the -600/0 ms time window, known as pN, and the BP over medial central sites. The second row maps show the topography of the P1 over visual areas. The third row displays the maps for the N1 component, which is more laterally localized than the P1. The last row shows the maps for the P2 component, which is very strong in all of the conditions over bilateral parieto-occipital sites. No topographical differences can be appreciated in any component across Conditions and Aerobic fitness.

DISCUSSION

The present study investigated premotor neurocognitive and early perceptual processing in preadolescent children to further our understanding of the relation of cardiorespiratory fitness to cognitive function within the preparation–perception–action cycle. Specifically, the findings indicated that aerobic fitness was selectively related to larger pN and P1 amplitude as well as better task performance. On the whole, the results show that the benefits of being aerobically fit start early in the processing stream during the performance of a task that challenges cognitive control, with differences observed at the stage of cognitive preparation of the behavioral response before the onset of the stimulus that triggers the response.

The participants were administered a modified version of a flanker task, which requires modulation of cognitive control and specifically challenges perceptual interference and response inhibition. At the behavioral level, aerobic fitness was related to accuracy, with higher fit children being more accurate than lower fit children. No significant group differences were observed for response times. These findings confirm the sensitivity of accuracy in task performance to the aerobic fitness status of preadolescent children in tasks that require cognitive control (Hillman et al., 2009; Pontifex et al., 2011; see also Hillman et al., 2011 for a review).

The current findings add novel evidence to neurocognitive pathways through which cardiovascular fitness leads to increased performance on tasks requiring the flexible modulation of cognitive control processes. Previous studies have demonstrated that cardiovascular fitness leads to more efficient modulation of attentional resource allocation (i.e., P3 amplitude) to the task conditions at later stages of stimulus processing. The present findings indicate that aerobic fitness also modulates brain activity early in the processing stream, specifically at pre-stimulus stages of motor preparation and very early stages of visual stimulus processing.

Specifically, we focused on the activity over the prefrontal cortex and the motor-related brain regions before stimulus onset. This is a novel approach, because, to our knowledge, no prior studies have looked at the cognitive-motor preparation processing in this age group during flanker task performance. The only prior studies focused on the motor preparation during self-paced movements (Warren and Karrer, 1984a,b) and did not employ an individual difference approach to the study of fitness. Indeed, the authors could not detect the typical BP component, but they observed a monophasic positive waveform preceding movement in

M. Berchicci et al. / Neuroscience 298 (2015) 211-219



Fig. 2. Three-dimensional topographical maps obtained in the time window of the considered components. The maps are displayed in the chronological order of the components from the top to the bottom (pN-BP, P1, N1, and P2), whereas the column of maps corresponds to the group.

preadolescents, whereas in younger children they showed a positive–negative–positive complex over the central sites starting 600–650 ms before the movement onset. We instead showed that the BP or readiness potential arising from the supplementary motor area is well detectable in this population and is similar in morphology to that of older participants obtained in different visuomotor tasks (Berchicci et al., 2013, 2014; Sánchez-López et al., 2014), but it is not modulated by aerobic fitness in this specific task. However, a more recent study (Kamijo et al., 2011) found that increased cardiorespiratory fitness is associated with improvements in the cognitive control of working memory in preadolescent children in the phase that precedes target stimulus onset, as reflected in larger CNV over frontal areas. Nonetheless, the relationship between prefrontal brain activity preceding the stimulus and the motor onset and cardiovascular fitness in preadolescents during a cognitive-motor task is not clear yet.

The involvement of the prefrontal areas is particularly important when high-order stimulus-responses rules (as in the present task) are required (Bunge and Zelazo, 2006; Lamm et al., 2006; Moore et al., 2014; see Tau and Peterson, 2010 for a review); its activity has been associated with proactive inhibitory control through which a "no-go" state is maintained prior to stimulus presentation, and the motor system is released from inhibition only if there is sufficient evidence for action (Di Russo et al., 2013). Although the development of prefrontal brain function is still a matter of debate (Tsujimoto, 2008), present results show that the prefrontal control is already present in 10-year-old children and it is enhanced by aerobic fitness. We have observed aerobic fitness-related differences selectively at a site over the prefrontal cortex during response preparation, with larger pN amplitude in higher compared to lower fit children, indicating enhanced cognitive preparation for the response. The observed differences extend to preadolescent children, indicating modulation of this component as a function of age and aerobic fitness in young, middle-aged and older adults (Berchicci et al., 2013, 2014).

The aerobic fitness-related modulation of brain function as early as the premotor stage gives further support to the hypothesis, raised by Pontifex et al. (2011) and further developed by Voss et al. (2011), that higher fit children are more likely to engage in proactive cognitive control, while their lower fit counterparts engage a more reactive control strategy. Our results may extend this explanation by adding that higher fit children optimize behavioral responses (i.e., higher fit are more accurated than lower fit) during cognitive control performance proactively, by means of a phasic engagement of cognitive processes for motor preparation prior to the onset of the taskrelevant stimulus (i.e., larger pN in higher than lower fit children). This proactive preparation that generalizes across task conditions would particularly benefit task performance in the more complex inconsistent condition (i.e.. larger pN in incompatible than compatible stimulus-response condition). The utilization of this proactive, phasic preparation strategy is made possible by more efficient cognitive control brain networks.

We have further showed modulation of the early perceptual components (i.e., P1 and N1) after stimulus onset as a function of aerobic fitness, unfolding different cognitive control strategies before and, consequently, after stimulus presentation. Amplitude of the ERP components related to visual processing mechanisms (P1 and N1) may be influenced by various factors (Moore et al., 2014). Among these, cardiovascular fitness induced by physical activity benefits visual information processing already at early stages, as evidenced by the modulation of the P1 component. It seems that higher fit children are able to draw more attention to task-relevant stimuli, as reflected in larger P1 amplitude, while lower fit children demonstrate less allocation of attentional resources in response to task conditions requiring cognitive control, regardless of complexity, as suggested by smaller P1 amplitude. Further, the N1 peak amplitude was modulated by the complexity of the task. The N1 is thought to index discriminative processing of visual stimuli and is modulated by attention (Baines et al., 2011). The discriminative processes required by the incompatible condition are more effortful than those needed to accomplish the more simplistic compatible condition, justifying the larger amplitude of the N1 component during the more challenging incompatible condition.

Collectively, the present findings linking aerobic fitness to pre- and early post-stimulus components of

the cognitive processing stream suggest that enhanced activity in the prefrontal brain areas may improve cognitive control in visuo-motor tasks allowing stronger proactive inhibition and greater allocation of selective attention on relevant external stimuli. These modulations in brain function could explain, in part, the beneficial relation of aerobic fitness to behavioral performance. In order to track qualitative and quantitative changes in functional brain circuitry across the life span, future research should collect data from older subjects (i.e., young and older adults) during the same task.

CONCLUSION

The present findings support the relevance of physical activity for the promotion of cognitive and brain health at a young age. Physical activity is a multidimensional behavior important for learning, enjoyment, social interaction and physiological health. The worldwide imbalance in the educational system in favor of sedentary learning at the expense of physical activity has implication not only for children's physical health (Malina, 2013), but also for their cognitive and brain health. The consistent evidence of a positive relationship between physical activity, aerobic fitness, cognitive and brain function and, consequently, academic performance (Kwak et al., 2009; Donnelly and Lambourne, 2011; Tomporowski et al., 2011) should motivate policy makers to develop opportunities for increasing physical activity in the classroom and across the school day (Mahar et al., 2006).

REFERENCES

- Ahn S, Fedewa AL (2011) A meta-analysis of the relationship between children's physical activity and mental health. J Pediatr Psychol 36:385–397.
- Baines S, Ruz M, Rao A, Denison R, Nobre AC (2011) Modulation of neural activity by motivational and spatial biases. Neuropsychologia 49:2489–2497.
- Berchicci M, Lucci G, Pesce C, Spinelli D, Di Russo F (2012) Prefrontal hyperactivity in older people during motor planning. NeuroImage 62:1750–1760.
- Berchicci M, Lucci G, Di Russo F (2013) Benefits of physical exercise on the aging brain: The role of the prefrontal cortex. J Gerontol. <u>http://dx.doi.org/10.1093/gerona/glt094</u>.
- Berchicci M, Lucci G, Perri RL, Spinelli D, Di Russo F (2014) Benefits of physical exercise on basic visuo-motor functions across age. Front Aging Neurosci. <u>http://dx.doi.org/10.3389/</u> <u>fnagi.2014.00048</u>.
- Braver TS, Gray JR, Burgess GC (2007) Explaining the many varieties of working memory variation: dual mechanisms of cognitive control. In: Conway A, Jarrold C, Kane M, Miyake A, editors. Variation in working memory. Oxford: Oxford University Press. p. 76–106.
- Buck SM, Hillman CH, Castelli DM (2008) The relation of aerobic fitness to Stroop task performance in preadolescent children. Med Sci Sports Exerc 40:166–172.
- Bunge SA, Zelazo PD (2006) A brain-based account of the development of rule use in childhood. Curr Direct Psychol Sci 15:118–121.
- Chaddock L, Erickson KI, Prakash RS, Kim JS, Voss MW, van Patter M, et al. (2010) A neuroimaging investigation of the association between aerobic fitness, hippocampal volume and memory performance in preadolescent children. Brain Res 1358:172–183.

- Chaddock L, Hillman CH, Buck SM, Cohen NJ (2011) Aerobic fitness and executive control of relational memory in preadolescent children. Med Sci Sports Exerc 43:344–349.
- Chatrian GE, Lettich E, Nelson PL (1985) Ten percent electrode system for topographic studies of spontaneous and evoked EEG activity. Am J EEG Technol 25:83–92.
- Colcombe SJ, Kramer AF, Erickson KI, Scalf P, McAuley E, Cohen NJ, et al. (2004) Cardiovascular fitness, cortical plasticity, and aging. Proc Natl Acad Sci USA 101:3316–3321. <u>http://dx.doi.org/10.1073/pnas.0400266101</u>.
- Crova C, Struzzolino I, Marchetti R, Masci I, Vannozzi G, Forte R, Pesce C (2014) Benefits of cognitively challenging physical activity in overweight children. J Sports Sci 32:201–211. <u>http:// dx.doi.org/10.1080/02640414.2013.828849</u>.
- Davis CL, Tomporowski PD, Mc Dowell JE, Austin BP, Miller PH, Yanasak NE, Allison JD, Naglieri JA (2011) Exercise improves executive function and achievement and alters brain activation in overweight children: a randomized, controlled trial. Health Psychol 30:91–98. <u>http://dx.doi.org/10.1037/a0021766</u>.
- Di Russo F, Lucci G, Sulpizio V, Berchicci M, Spinelli D, Pitzalis S, Galati G (2013) Spatiotemporal mapping of response inhibition in the prefrontal cortex. Neuropsychological Trends 79. ISSN 1970-321X.
- Donnelly JE, Lambourne K (2011) Classroom-based physical activity, cognition, and academic achievement. Prev Med 52:S36–S42.
- Erickson KI, Gildengers AG, Butters MA (2013) Physical activity and brain plasticity in late adulthood. Dialogues Clin Neurosci 15:99–108.
- Eriksen BA, Eriksen CW (1974) Effects of noise letters upon the identification of a target letter in a non search task. Percept Psychophysiol 16:143–149.
- Faul F, Erdfelder E, Lang A-G, Buchner A (2007) G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 29:175–191. <u>http://dx.doi.org/10.3758/BF03193146</u>.
- Fedewa AL, Ahn S (2011) The effects of physical activity and physical fitness on children's achievement and cognitive outcomes: a meta-analysis. Res Q Exerc Sport 82:521–535.
- Friedman D, Nessler D, Cycowicz YM, Horton C (2009) Development of and change in cognitive control: a comparison of children, young and older adults. Cogn Affect Behav Neurosci 9:91–102.
- Gratton G, Coles MGH, Donchin E (1983) A new method for off-line removal of ocular artifact. Electrophysiol Clin Neurophysiol 55:468–484.
- Hillman CH, Castelli DM, Buck SM (2005) Aerobic fitness and neurocognitive function in healthy preadolescent children. Med Sci Sports Exerc 37:1967–1974.
- Hillman CH, Kramer AF, Belopolsky AV, et al. (2006) A crosssectional examination of age and physical activity on performance and event-related brain potentials in a task switching paradigm. Int J Psychophysiol 59:30–39.
- Hillman CH, Erickson KI, Kramer AF (2008) Be smart, exercise your heart: exercise effects on brain and cognition. Nat Rev Neurosci 9:58–65.
- Hillman CH, Buck SM, Themanson JR, et al. (2009) Aerobic fitness and cognitive development: event-related brain potential and task performance indices of executive control in preadolescent children. Dev Psychol 45:114–129.
- Hillman CH, Kamijo K, Scudder M (2011) A review of chronic and acute physical activity participation on neuroelectric measures of brain health and cognition during childhood. Prev Med 52:S21–S28.
- Hillman CH, Pontifex MB, Castelli DM, Khan NA, Raine LB, Scudder MR, et al. (2014) Effects of the FIT kids randomized controlled trial on executive control and brain function. Pediatrics 134:1063–1071. <u>http://dx.doi.org/10.1542/peds.2013-3219</u>.
- Kamijo K, O'Leary K, Pontifex MB, Themanson JR, Hillman CH (2010) Aerobic fitness effects on neuroelectric indices of cognitive and motor task performance. Psychophysiology 47:814–821.
- Kamijo K, Pontifex MB, O'Leary K, Scudder MR, Wu CT, Castelli DM, Hillman CH (2011) The effects of an afterschool physical activity program on working memory in preadolescent children. Dev Sci 1–13. http://dx.doi.org/10.1111/j.1467-7687.2011.01054.x.

- Keeley TJH, Fox KR (2009) The impact of physical activity and fitness on academic achievement and cognitive performance in children. Int Rev Sport Exerc Psychol 2(2):198–214. <u>http://dx.doi.org/</u> <u>10.1080/17509840903233822</u>.
- Krafft CE, Schwarz NF, Chi L, Weinberger AL, Schaeffer DJ, Pierce JE, et al. (2014) An 8-month randomized controlled exercise trial alters brain activation during cognitive tasks in overweight children. Obesity 22:232–242. <u>http://dx.doi.org/10.1002/obv.20518</u>.
- Kwak L, Kremers SPJ, Bergman P, Ruiz JR, Rizzo NS, Sjostrom M (2009) Associations between physical activity, fitness, and academic achievement. J Pediatrics 155:914–918.
- Lamm C, Zelazo PD, Lewis MD (2006) Neural correlates of cognitive control in childhood and adolescence: disentangling the contribution of age and executive function. Neuropsychologia 44:2139–2148.
- Mahar MT, Murphy SK, Rowe DA, Golden J, Shields AT, Raedeke TD (2006) Effects of a classroom-based program on physical activity and on-task behavior. Med Sci Sports Exerc 38:2086–2094.
- Malina RM (2013) Top 10 research questions related to growth and maturation of relevance to physical activity, performance, and fitness. Res Q Exerc Sport 85:157–173.
- Moore RD, Drollette ES, Scudder MR, Bharij A, Hillmann CH (2014) The influence of cardiorespiratory fitness on strategic, behavioral, and electrophysiological indices of arithmetic cognition in preadolescent children. Front Hum Neurosci. <u>http://dx.doi.org/</u> <u>10.3389/fnhum.2014.00258</u>.
- Oldfield RC (1971) The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 104:199–206.
- Perri RL, Berchicci M, Spinelli D, Di Russo F (2014a). Individual differences in response speed and accuracy are associated to specific brain activities of two interacting systems. Front Behav Neurosci, in press. <u>http://dx.doi.org/10.3389/fnbeh.2014.0025</u>.
- Perri RL, Berchicci M, Lucci G, Spinelli D, Di Russo F (2014b). The premotor role of the prefrontal cortex in response consistency. Neuropsychology. <u>http://dx.doi.org/10.1037/neu0000168</u>.
- Polich J (2007) Updating P300: an integrative theory of P3a and P3b. Clin Neurophysiol 118:2128–2148.
- Pontifex MB, Hillman CH (2007) Neuroelectric and behavioral indices of interference control during acute cycling. Clin Neurophysiol 118:570–580.
- Pontifex MB, Hillman CH, Polich J (2009) Age, physical fitness, and attention: P3a and P3b. Psychophysiology 46:379–387.
- Pontifex MB, Raine LB, Johnson CR, Chaddock L, Voss MW, Cohen NJ, et al. (2011) Cardiorespiratory fitness and the flexible modulation of cognitive control in preadolescent children. J Cogn Neurosci 23:1332–1345.
- Raine LB, Lee HK, Saliba BJ, Chaddock-Heyman L, Hillman CH, et al. (2013) The influence of childhood aerobic fitness on learning and memory. PLoS One 8:e72666. <u>http://dx.doi.org/10.1371/journal.pone.0072666</u>.
- Sánchez-López J, Fernández T, Silva-Pereyra J, Martínez Mesa JA, Di Russo F (2014) Differences in visuo-motor control in skilled vs. novice martial arts athletes during sustained and transient attention tasks: a motor-related cortical potential study. PLoS One 9:91112.
- Shibasaki H, Hallett M (2006) What is Bereitschaftspotential? Clin Neurophysiol 117:2341–2356.
- Shvartz E, Reibold RC (1990) Aerobic fitness norms for males and females aged 6 to 75 years: a review. Aviat Space Environ Med 61:3–11.
- Spencer KM, Coles MGH (1999) The lateralized readiness potential: relationship between human data and response activation in a connectionist model. Psychophysiology 36:364–370.
- Stroth S, Kubesch S, Dieterle K, Ruchsowd M, Heim R, Kiefer M (2009) Physical fitness, but not acute exercise modulates eventrelated potential indices for executive control in healthy adolescents. Brain Res 1269:114–124.
- Tau GZ, Peterson BS (2010) Normal development of brain circuits. Neuropsychopharmacology 35:147–168.

- Tomporowski PD, Lambourne K, Okumare MS (2011) Physical interventions and children's mental function: an introduction and overview. Prev Med 52:S3–S9.
- Tsujimoto S (2008) The prefrontal cortex: functional neural development during early childhood. Neuroscientist 14:345–358.
- Verleger R, Jaskowski P, Wascher E (2005) Evidence for an integrative role of P3b in linking reaction to perception. J Psychophysiol 19:165–181.
- Voss MW, Chaddock L, Kim JS, Vanpatter M, Pontifex MB, Raine LB, Cohen NJ, Hillman CH, Kramer AF (2011) Aerobic fitness is associated with greater efficiency of the network underlying cognitive control in preadolescent children. Neuroscience 199:166–176.
- Warren CA, Karrer R (1984a) Movement-related potentials during development: a replication and extension of relationships to age, motor control, mental status and IQ. Int J Neurosci 24:81–96.

- Warren CA, Karrer R (1984b) Movement related potentials in children. A replication of waveforms, and their relationships to age, performance and cognitive development. Ann N Y Acad Sci 425:489–495.
- Wu CT, Pontifex MB, Raine LB, Chaddock L, Voss MW, Kramer AF, Hillman CH (2011) Aerobic fitness and response variability in preadolescent children performing a cognitive control task. Neuropsychology 25:333–341. <u>http://dx.doi.org/10.1037/</u> a0022167.
- Zwierko T, Lubinski W, Lesiakowski P, Steciuk H, Piasecki L, Krzepota J (2014) Does athletic training in volleyball modulate the components of visual evoked potentials? A preliminary investigation. J Sport Sci. <u>http://dx.doi.org/10.1080/</u> 02640414.2014.903334.

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