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Greater childhood cardiorespiratory fitness is associated with better top-down cognitive control: A midfrontal theta oscillation study

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Abstract

The aim of the current study was to examine the association between cardiorespiratory fitness and electroencephalogram-based neural oscillations, using midfrontal theta, during an inhibitory control task in children. One-hundred seventy-one school-aged children (mean age = 8.9 ± 0.6 years; 46% girls) were recruited. Cardiorespiratory fitness was assessed by a test of maximal oxygen consumption (VO_{2peak}) while inhibitory control performance was measured via a modified flanker task with an electroencephalogram. Behavioral findings demonstrated that higher cardiorespiratory fitness was associated with higher response accuracy regardless of task difficulty as well as lower response variability during trials with lower cognitive demand. Neuroelectric outcomes revealed that higher cardiorespiratory fitness was correlated with smaller modulation of theta (4–7 Hz) oscillatory power regardless of task difficulty. Collectively, the current findings indicate that higher cardiorespiratory fitness is associated with better performance on a task that modulates inhibitory control, signified by higher, and more stable, task performance. More importantly, higher childhood cardiorespiratory fitness is associated with better top-down control and cortical communication, as reflected by midfrontal theta. Such findings support the critical role of cardiorespiratory fitness in brain health during childhood.

KEYWORDS

EEG, fitness, oscillatory brain rhythms, time-frequency analysis, top-down control

1 | INTRODUCTION

The prevailing trend of physical inactivity in children has become a global health issue due to changes in transportation habits and increased use of technology, among other factors. According to a 2018 report across 49 countries, approximately 75% of school children are considered sedentary worldwide (Children's Hospital of Eastern Ontario Research Institute, 2018). This issue is a relevant public health concern given that numerous studies have observed detrimental effects of physical inactivity and poor physical fitness on cardiometabolic health (Eisenmann, 2003) and cognitive functioning (Erickson et al., 2019; Physical Activity Guidelines Advisory Committee, 2018) during childhood.

Of note, the current literature indicates a link between increased cardiorespiratory fitness and brain health in children, with a small to moderate relationship of cardiorespiratory fitness on inhibitory control at a cognitive/attention level (Berchicci et al., 2015; Raine et al., 2018; Scudder et al., 2014; Wu et al., 2011; Zhan et al., 2020). Inhibitory control refers to the cognitive ability to withhold an individual's attention to respond to irrelevant but prepotent information and stay focused on goal-relevant information (Diamond, 2013). The impact of this relationship is enhanced by recent meta-analyses of experimental evidence showing that forms of aerobic exercise that target cardiorespiratory fitness have led to improved higher order cognition, including inhibitory control, in children (Ludyga, Gerber, Pühse, Looser, & Kamijo, 2020; Xue, Yang, & Huang, 2019). Better inhibitory control in childhood has educational implications given that this cognitive domain plays a vital role in children's learning and their ability to navigate busy classroom environments (Hillman et al., 2012). Interestingly, a large-scale study indicated that the relationship between cardiorespiratory fitness and inhibitory control is stronger in task conditions that necessitate greater cognitive demand (i.e., incongruent trials), relative to conditions with lower cognitive demand (i.e., congruent trials), during different versions of flanker tasks (Raine et al., 2018).

Beyond behavioral assessments, it may be informative to utilize electrophysiological assessments, including electroencephalography (EEG) frequency dynamics, to assess the relationship between cardiorespiratory fitness and childhood brain health. Here, we conducted a time-frequency analysis of EEG, which provides insights into the temporal dynamics of the magnitude of EEG, including neural synchronization and desynchronization (a state of synchrony/desynchrony in a population of neurons) at specific frequency bands that relate to events of interest (Klimesch, 1999; Makeig, Debener, Onton, & Delorme, 2004). Accordingly, frontal midline theta (termed "midfrontal theta" hereafter) is a neural marker of the frontal-mediated top-down control processes (Cavanagh & Frank, 2014). It is well documented that theta oscillations over the medial-frontal regions (i.e., medial prefrontal cortex [mPFC], anterior cingulate cortex [ACC]) are sensitive to stimulus novelty and stimulus-response conflict, and is evoked when individuals perceive a need for enhanced control processes to adaptively change behavior (Cavanagh & Frank, 2014). Stated differently, there is a close relationship between increased midfrontal theta power and signaling of higher cognitive control demand in novel and conflicting situations. Moreover, other studies indicate that midfrontal theta is also associated with the orchestration of online monitoring and adaptation of task performance, in which the medial frontal cortex signals and communicates with long-range task-relevant cortical areas (e.g., lateral prefrontal cortex, motor cortex, parietal cortex, and somatosensory cortex) responsible for top-down sensory-motor decision making, inhibition, and attention when cognitive control is needed (Cavanagh & Frank, 2014; Cohen & Donner, 2013; Duprez, Gulbinaite, & Cohen, 2020).

Previous studies on the association between cardiorespiratory fitness and theta oscillation have shown inconsistent findings in adults. For example, Wang and colleagues indicated that higher fit adults had larger theta oscillatory power in a midline cluster (i.e., Fz, FCz, Cz, CPz, and Pz) during a visuospatial attention-cueing task relative to lower fit adults, regardless of task difficulty (Wang et al., 2015). However, Chaire, Becke, and Düzel (2020) found null effects of an aerobic exercise intervention on theta oscillation using a frontal-parietal cluster (i.e., Fz, F3, F4, Pz, P3, and P4) during a visual attention search task and a working memory task. Of note, neither study specifically focused on midfrontal theta, leaving the association of increased cardiorespiratory fitness with midfrontal theta oscillation unknown.

Moreover, it is worthwhile to expand the investigation to children given that the cognitive implications of midfrontal theta may be particularly relevant during development. Specifically, research on indivudal differences has revealed greater midfrontal theta power in children with developmental disorders (e.g., attention-deficit/hyperactivity disorder [ADHD], autism spectrum disorder [ASD]) relative to their typically developing counterparts during various cognitive operations, suggesting that children with developmental disorders may "overtax" top-down control during task execution (Kawasaki et al., 2017; Lenartowicz et al., 2014). Such excessive involvement of midfrontal theta during top-down control may result from maldevelopment of the frontal cortex (Shaw et al., 2013) and its associated cognitive processes (e.g., stimulus encoding; Lenartowicz et al., 2014). Furthermore, Kawasaki et al. (2017) indicated that greater midfrontal theta power was associated with higher severity of ASD symptoms, whereas no association was found between midfrontal theta oscillation and performance of a motor tapping task. Findings stemming from the abovementioned research, therefore, may suggest a unique role of midfrontal theta in probing maladaptive cognitive development and/or symptoms of developmental disorders that cannot be addressed by behavioral assessments. Given that cardiorespiratory fitness could be associated with modulations in mPFC (Herting & Nagel, 2013) and/or ACC (Chaddock et al., 2012; Voss et al., 2011), two brain regions that underpin midfrontal theta and top-down control, in children, and further studies have suggested that midfrontal theta reflects a neural mechanism underlying coordination of cognitive processes involved in immature top-down control to support performance on inhibition-related tasks in children (Adam, Blaye, Gulbinaite, Delorme, & Farrer, 2020), investigation into whether greater cardiorespiratory fitness is associated with favorable modulation (i.e., smaller oscillatory power) in midfrontal theta during an inhibitory control task in healthy children is relevant to understanding whether such processes are modifiable by health-related factors and lifestyle behaviors.

Accordingly, the aim of the current study was to investigate the association between cardiorespiratory fitness and midfrontal theta oscillations evoked by a flanker task in children, and to seek whether midfrontal theta oscillation mediates the relationship between cardiorespiratory fitness and inhibitory control task performance. Based on the literature summarized above, it was hypothesized that higher cardiorespiratory fitness would be associated with smaller midfrontal theta oscillation, reflecting better top-down control and cortical communication, in children regardless of task demand. We further hypothesized that higher fitness would be associated with better flanker task performance, as reflected generally by better performance across congruency trials and selectively via a stronger association of fitness with incongruent trials relative to congruent trials. Moreover, we hypothesized that midfrontal theta oscillation would mediate the relationship between fitness and performance on a flanker task. Overall, the current investigation stands to provide additional evidence for the critical role of cardiorespiratory fitness in facilitating brain health during childhood.

2 | METHOD

The current study was a secondary analysis of a subset of data from the FITKids intervention trial (ClinicalTrials.gov: NCT01619826; Hillman et al., 2014), with only data from baseline measures investigated. The novel aim of this secondary analysis was the relationship between cardiorespiratory fitness and midfrontal theta oscillation, and whether midfrontal theta may mediate the relationship between fitness and performance on a flanker task. The portion of the task performance data (i.e., response accuracy findings) reported herein that overlap with baseline data from Hillman et al. (2014) were presented only to better inform the midfrontal theta findings.

2.1 | Participants

A total of 171 healthy preadolescent children between the ages of 8 to 9 years were recruited from East-Central Illinois for this analysis. This sample was drawn from an original sample of 221 participants from the FITKids intervention trial. Of the original 221 participants, 50 were excluded because of (a) missing baseline EEG data ($n = 8$), (b) poor EEG data quality ($n = 20$), (c) not meeting VO_{2peak} test criteria ($n = 20$; see Section 2.3 for detail of criteria), or d) having <50% of overall response accuracy in the cognitive task ($n = 2$; Westfall, Kao, Scudder, Pontifex, & Hillman, 2017). Participants and their legal guardian signed informed assent and consent forms approved by the Institutional Review Board of the University of Illinois at Urbana-Champaign. Guardians were asked to complete a health history and demographics questionnaire as well as other documentation, indicating that their child: (a) had normal or corrected-to-normal vision, (b) was free of neurological diseases (e.g., attention deficit/hyperactivity disorders) and/or did not have an individual education plan related to developmental or attention disorders based on parental disclosure, and (c) had no physical disabilities that could be exacerbated by exercise participation (Physical Activity Readiness Questionnaire [PARQ]; Thomas, Reading, & Shephard, 1992). Table 1 summarizes demographic and anthropometric data of participants.

TABLE 1 Demographic data of participants

Variables	*M* (*SD*)	Range
N	171 (46% girls)	
Age (years)	8.9 (0.6)	8.0–9.9
Puberty stage	1.4 (0.5)	1.0–2.5
BMI ($kg.m^{-2}$)	19.0 (4.0)	13.0–31.0
BMI percentile (%)	68.5 (27.2)	1–100
IQ	105 (9.8)	84–128
SES	1.94 (0.9)	1–3
VO_{2peak} ($ml.kg^{-1}.min^{-1}$)	38.4 (6.9)	19.9–53.2
VO_{2peak} percentile (%)*	19.3 (20.9)	3–83

*Only 4% of children had VO_{2peak}% >75th percentile score and 76% of children had VO_{2peak}% <25th percentile score.

2.2 | Procedure

On the first visit, demographic information including age, gender, pubertal stage, socioeconomic status (SES), intelligence quotient (IQ), and body mass index (BMI) were collected. Age and gender were verbally disclosed by a legal guardian. For pubertal stage, legal guardians provided ratings on a 5-point Tanner scale, with 1 indicating a prepubertal state and 5 indicating the full mature state (Taylor et al., 2001). Parental ratings on this scale have acceptable validity in differentiating between prepubertal and pubertal status (Rasmussen et al., 2015). SES was determined using a trichotomous index based on the following: (a) participation in free or reduced-price meal program at school, (b) the highest level of education obtained by the parents, and (c) number of parents who worked full-time (Birnbaum et al., 2002). Participants also completed the Kaufman Brief Intelligence Test (K-BIT; Kaufman & Kaufman, 1990) to assess IQ, and the PARQ to screen for health issues that may be exacerbated by physical exercise. Afterwards, participants were then fit with a Polar heart rate (HR) monitor (Model A1, Polar Electro, Finland), had their height and weight measured, and completed a maximal exercise test to assess cardiorespiratory fitness. BMI was calculated as an individual's weight divided by their height in meters squared, and BMI percentiles were further computed using Centers for Disease Control and Prevention growth charts (Kuczmarski et al., 2000). On the second visit, participants performed a modified flanker task to assess inhibitory control with concurrent neuroelectric assessment, and received $10/hr for their participation.

2.3 | Cardiorespiratory fitness assessment

Cardiorespiratory fitness was assessed using a test of maximal oxygen consumption (VO_{2peak}) measured on a motor-driven treadmill following a modified Balke protocol (American College of Sports Medicine [ACSM], 2010). This test employed a computerized indirect calorimetry system (TrueMax 2400; Parvo Medics, Sandy, UT, USA) while participants walked/ran on a motor-driven treadmill at a constant speed with a 2.5% incremental grade increase every 2-min until volitional exhaustion. A Polar heart rate (HR) monitor (Model A1; Polar Electro, Finland) was used to measure HR throughout the test. Ratings of perceived exertion (RPE) were assessed every 2 min with the children's OMNI scale (a pictorial 10-point Likert scale ranging from “not at all tired” to “very, very tired”; Utter, Robertson, Nieman, & Kang, 2002). Relative peak oxygen consumption (VO_{2peak}) was expressed in $ml.kg-^{1}.min-^{1}$ and was based upon maximal effort as evidenced by: (a) a VO_2 plateau corresponding to an increase of less than 2 $ml.kg^{-1}.min^{-1}$ despite an increase in workload; (b) a peak heart rate ≥185 beats per minute (ACSM, 2010) or a HR plateau (Freedson & Goodman, 1993); (c) Respiratory exchange ratio ≥1.0 (Bar-Or, 1983); and/or (d) ratings on the children's OMNI scale of perceived exertion ≥8 (Utter et al., 2002). Participants had to either reach a VO_2 plateau or had to meet at least two of the three remaining confidence criteria when VO_2 plateau was not reached. To standardize scores, VO_{2peak} percentile (VO_{2peak}%) was determined based on individuals’ age, gender, and relative scores from normative data (Shvartz & Reibold, 1990).

2.4 | Inhibitory control task

Inhibitory control was assessed using a modified Eriksen flanker task (Eriksen & Eriksen, 1974). All stimuli were presented focally at a distance of ~1 meter using Neuroscan Stim software version 4.5 (Compumedics, Charlotte, NC) and consisted of a child-friendly goldfish graphic amid bilaterally flanking goldfish. Flanking stimuli were either stimulus-congruent (i.e., facing the same direction) or stimulus-incongruent (i.e., facing the opposite direction) to the central target stimulus. Stimuli, presented on a blue background, were 3 cm tall and appeared for 200 ms with a fixed inter-trial interval of 1,700 ms. Participants were instructed to respond using a response pad as quickly and accurately as possible with a thumb press according to the directionality of the centrally presented target fish amid either congruous (swimming in the same direction) or incongruous (swimming in the opposite direction) flanking fish. Stimulus-congruency was varied by manipulating the direction of the flanking fish in relation to the central target fish. Two blocks of 75 trials with equiprobable stimulus-congruent and stimulus-incongruent trials were administered with participants. Forty practice trials were provided prior to each condition. Trials with incorrect responses or reaction time <150 ms or >1,000 ms were discarded. Response accuracy, mean reaction time (mean RT) of correct-response trials, standard deviation of RT (SDRT), and coefficient of variation of RT (CVRT; SDRT/mean RT) were calculated as behavioral outcomes.

2.5 | Neuroelectric Assessment

Electroencephalographic (EEG) activity was recorded from 64 electrode sites arranged according to the international 10–10 system using a Neuroscan EEG Quik-Cap (Compumedics, Charlotte, NC). All electrodes maintained an impedance <10kΩ prior to EEG recordings. Continuous data were referenced online using CCPz with AFz electrode serving as the ground. Additional electrodes were placed above and below the left orbit and outer canthus of each eye to monitor electrooculographic (EOG) activity. Continuous data were digitalized at a sampling rate of 500 Hz, amplified 500 times with a DC-to-70 Hz filter, and a 60-Hz notch filter was applied using a Neuroscan SynAmps2 amplifier. Matlab (R2019a, Mathworks Inc.), EEGLAB toolbox (version 2019.0, Delorme & Makeig, 2004), and ERPLAB toolbox (version 7.0.0, Lopez-Calderon & Luck, 2014) were used for offline data processing. Continuous data were re-referenced to averaged mastoids (M1, M2), followed by independent component analysis and an automated eyeblink component removal procedure (Pontifex, Gwizdala, Parks, Billinger, & Brunner, 2017). Afterwards, continuous EEG data were segmented into epochs from −1,500 to 1,500 ms time-locked to stimulus onset (Wang, Yang, Moreau, & Muggleton, 2017), which were baseline corrected using the entire sweep (Chang, Chu, Wang, Song, Wei, 2015). Trials with incorrect responses and those containing artifacts with amplitudes exceeding ±150 μV were discarded. The data were then exported to the EEGLAB toolbox to analyze the event-locked theta responses. The average number of epochs included in the analyses were 57.0 ± 7.4 and 54.3 ± 7.9 for congruent and incongruent trials, respectively.

2.6 | Time-frequency analysis

The EEGLAB toolbox was utilized to analyze the event-locked theta responses. A Morlet-based wavelet transform with a width of three cycles was employed to provide a continuous measure of the amplitude of a frequency component between −1,000 and 1,000 ms relative to stimulus onset (EEGLAB; Delorme & Makeig, 2004). Event-related spectral permutations were computed on the wavelet-transformed epochs for each stimulus condition at each time point and wavelet frequency to yield time-frequency maps. Oscillatory power (the magnitude of the analyzed signal) was then averaged across trials. The averaged oscillatory power of each task condition for each participant was rescaled by the baseline values from −500 to −300 ms relative to stimulus onset (Nigbur, Cohen, Ridderinkhof, & Stürmer, 2012), and taking the log10 transform of this quotient (dB) (dB power = 10 × 10 [power/baseline]), allowed a direct comparison of results of interest across frequencies. The mean power in the time interval between 100 and 500 ms at 4–7 Hz (Wang et al., 2015; Yeung, Han, Sze, & Chan, 2016) for theta was extracted. We chose the 100–500 ms interval based on our time-frequency plots across all 171 participants (Supplementary Figure S1) and to avoid any spectral leakage from response execution (mean RTs >500 ms across congruency trials). We collapsed mean theta power from the frontal cluster (i.e., Fz, FCz) for statistical analysis. This decision was made by referring to previous study (Kao, Wang, & Hillman, 2020) and results from preliminary analysis showing that the Fz and FCz had greater overall theta power relative to Cz, CPz, and Pz (p's <.012), whereas no differences between the latter three sites (p's >.600) (Figure 1). These results support that theta oscillations during the 100–500 ms interval are driven by the midfrontal region. Figure 2 depicts the median-split plots of midfrontal theta oscillations as a function of cardiorespiratory fitness (median value of VO_{2peak}% = 11th percentile score).

2.7 | Statistical analysis

Five participants (2.9% of the sample) had missing demographic information (i.e., puberty stage [$N = 1$], SES [$N = 2$], and IQ [$N = 2$]). The data for these participants were imputed as the mean of the entire sample. In addition, data on VO_{2peak}% were normalized using log10-transformed method (presented as logVO_{2peak}% hereafter) because the data were

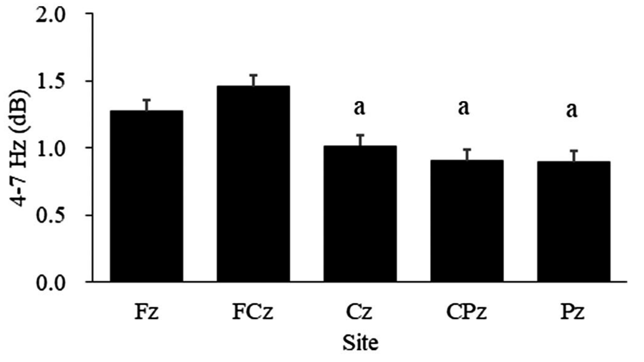

FIGURE 1 Theta oscillatory power (mean ± 1 SE) at the midline electrode sites. Data are collapsed across congruency trials. Overall theta power at Fz and FCz were higher than Cz, CPz, and Pz. Values sharing a common letter are not statistically different, p <.05

heavily skewed toward low-fit children (only 4% of children had VO_{2peak}% >75th percentile score and 76% of children had VO_{2peak}% <25th percentile score; see Supplementary Figure S2). Data were analyzed using the Statistical Package for the Social Sciences (version 24; SPSS) with an alpha threshold for all tests set at p = .05. For flanker task manipulation check, paired t tests were performed on response accuracy, mean RT, SDRT and CVRT, and midfrontal theta power. Next, preliminary bivariate Pearson correlation coefficients were computed between demographic variables (i.e., age, gender, pubertal stage, BMI%, IQ, and SES), cardiorespiratory fitness (logVO_{2peak}%) and behavioral (i.e., response accuracy, mean RT, SDRT, and CVRT) or EEG outcomes (i.e., midfrontal theta power). Demographic variables that were significantly associated with a specific behavioral or EEG outcomes were then entered as nuisance variables in subsequent regression models. For example, if age was significantly related to response accuracy but not midfrontal theta power during incongruent trials, it was only entered in the regression models predicting incongruent response accuracy but not incongruent theta power. Separate linear hierarchical regression analyses were performed using behavioral or EEG measures that were significantly correlated with cardiorespiratory fitness. Cardiorespiratory fitness was entered into step 2 in separate hierarchical regression analyses after the inclusion of nuisance variables into step 1. Assumptions of linearity, equality of variance, independence, and normality were plotted, inspected, and verified using fitted versus residual and Q-Q plots. Individual data points with standardized regression residuals >|3| and Cook's distance ≥1 would be considered as influential outliers (Pindus et al., 2018). Based on these criteria, no further case was excluded from the analyses. No multicollinearity was observed among any of the independent variables (VIF < 10). Moreover, once significant associations between cardiorespiratory fitness and neuroelectric/behavioral outcomes were observed, we

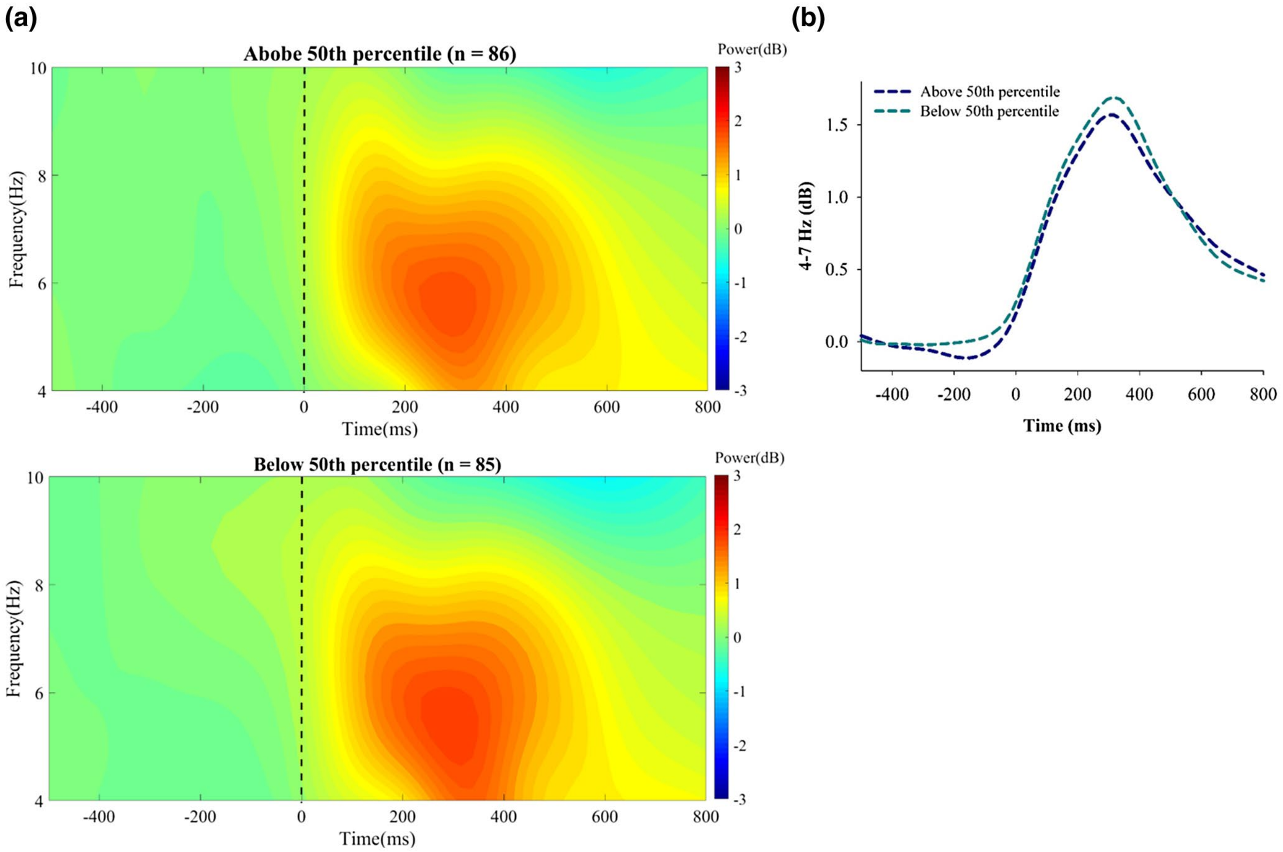

FIGURE 2 Median-split plots of midfrontal theta oscillations. Figure 2(a) depicts time-frequency plots of theta oscillations at the frontal cluster (Fz, FCz). Theta synchronization is depecited as power increase between 100 and 500 ms at 4–7 Hz relative to baseline (−500 to −300 ms). Figure 2(b) shows the difference between children with VO_{2peak}% above 50th percentile (n = 86) and children with VO_{2peak}% below 50th percentile (n = 85) on theta osicllatory power over time

assessed whether midfrontal theta mediated the relationship between cardiorespiratory fitness and the behavioral outcomes per established criteria in the method from Sobel and colleagues (Baron & Kenny, 1986; Sobel, 1982).

3 | RESULTS

3.1 | Task manipulation check

Separate paired t test revealed significant difference between stimulus congruency trials in response accuracy (t(170) = 12.52, p <.001; congruent: 81.7 ± 11.7% vs. incongruent: 75.2 ± 11.2%), mean RT (t(170) = 11.23, p <.001; congruent: 509.1 ± 108.9 ms vs. incongruent: 537.5 ± 119.4 ms), SDRT (t(170) = 6.64, p <.001; congruent: 151.3 ± 50.3 ms vs. incongruent: 167.9 ± 55.9 ms), and CVRT (t(170) = 3.85, p <.001; congruent: 29.1 ± 7.5% vs. incongruent: 30.7 ± 8.3%), suggesting successful task manipulation in which participants responded slower and less accurately to incongruent relative to congruent trials. In terms of midfrontal theta power, analyses showed no difference between stimulus congruency trials in theta power (t(170) = 0.75, p>.05; congruent: 1.26 ± 1.15 dB vs. incongruent: 1.32 ± 1.11 dB). Thus, theta power was collapsed across congruency trials in further analyses. See

TABLE 2 Summary of behavioral and EEG outcomes of flanker task

Variables	*M* (*SD*)	Range
Congruent trials		
Response Accuracy (%)	81.7 (11.7)	46.7–100.0
RT (ms)	509.1 (108.9)	289.7–801.1
SDRT (ms)	151.3 (50.3)	57.2–296.7
CVRT (%)	29.1 (7.5)	13.0–66.0
Theta power (dB)	1.26 (1.15)	−2.87–4.34
Incongruent trials		
Response Accuracy	75.2 (11.2)	43.2–98.7
RT (ms)	537.5 (119.4)	278.2–871.1
SDRT (ms)	167.9 (55.9)	61.8–306.8
CVRT (%)	30.7 (8.3)	15.0–54.0
Theta power (dB)	1.32 (1.11)	−1.93–3.67

Table 2 for a summary of behavioral and neuroelectric outcomes.

3.2 | Bivariate correlations

Table 3 summarizes results of the preliminary bivariate correlations. The results showed that age was significantly correlated with behavioral and EEG outcomes, including congruent accuracy (r =.24) and incongruent accuracy (r = .21), congruent RT (r = −.23) and incongruent RT (r = −.20), congruent SDRT (r = −24) and incongruent SDRT (r = −.22), congruent CVRT (r = −.16), and theta power (r = .15). IQ was also consistently correlated with behavioral outcomes, including congruent accuracy (r = .16), congruent RT (r = −.15), congruent SDRT (r = −.22), incongurent SDRT (r = −.29), congruent CVRT (r = −.19), and incongruent CVRT (r = −.25). Accordingly, age and IQ were entered into step 1 of hierarchical regression analyses on beahavioral measures while age was entered into step 1 of regression analysis on theta power. Furthermore, cardiorespiratory fitness was correlated with congruent accuracy (r = .16), incongruent accuracy (r = .17), congruent SDRT (r = −.16), congruent CVRT (r = −.16), and theta power (r = −.31).

3.3 | Hierarchical regression analyses

Table 4 summarizes the results of the hierarchical regression analyses. For response accuracy measures, hierarchical regression analyses revealed that children with higher cardiorespiaotry fitness exhibited higher congruent accuracy (β = .16, pr = .16, p = .034, t = 2.14) and higher incongruent accuracy (β = .17, pr = .17, p = .025, t = 2.25) (Table 4, Figure 3) after adjusting for age and IQ. Hierarchical regression analyses also revealed that higher cardiorespiratory fitness was associated with smaller congruent SDRT (β = −.14, pr = −.15, p = .049, t = −1.98) and was marginally associated with smaller congruent CVRT (β = −.15, pr = −.15, p = .052, t = −1.96) after adjusting for age and IQ (Table 4, Figure 3). Regarding midfrontal theta power, regression analysis indicated that children with higher cardiorespiraotry fitness had smaller overall frontal theta power (β = −.31, pr = −.30, p <.001, t = −4.14) after adjusting for age (Table 4, Figure 3).

3.4 | Mediation analysis

Given the above results, a mediation analysis was conducted to determine if smaller overall midfrontal theta power mediated the relationship between higher cardiorespiratory fitness and higher overall response accuracy or lower congruent SDRT/CVRT. Three conditions must be met to conduct a mediation analysis. First, the independent variable (fitness) must be associated with the dependent variable (overall response accuracy, congruent SDRT, or incongruent CVRT). Second, the independent variable must be associated with the mediator (midfrontal theta). Third, the mediator must be associated with the dependent variable (Baron & Kenny, 1986; Sobel, 1982).

However, even though cardiorespiratory fitness was significantly correlated with overall midfrontal theta power (r = −.31, p <.001), overall response accuracy (r = .18, p = .021), congruent SDRT (r = −.16, p = .038), and congruent CVRT (r = −.16, p = .037), there was no association between overall midfrontal theta power and any of the dependent variables (i.e., overall response accuracy, congruent SDRT, or congruent CVRT) (r's = −.04 − −0.01, p's > .63). As such, these correlations did not support our intention to perform the mediation analyses. Therefore, midfrontal theta is unlikely to

TABLE 3 Bivariate correlations between demographic variables, cardiorespiratory fitness, and behavioral and EEG outcomes

Variables	Age	Gender	Puberty	BMI%	SES	IQ	Fitness
Behavioral outcomes							
Congruent accuracy	**0.24***	−0.05	−0.11	0.01	0.08	**0.16***	**0.16***
Congruent RT	**−0.23***	−0.08	−0.03	−0.03	−0.02	**−0.15***	−0.02
Congruent SDRT	**−0.24***	−0.02	0.04	0.01	−0.06	**−0.22***	**−0.16***
Congruent CVRT	**−0.16***	0.04	0.08	−0.01	−0.05	**−0.19***	**−0.16***
Incongruent Accuracy	**0.21***	−0.03	−0.05	−0.02	0.07	0.12	**0.17***
Incongruent RT	**−0.20***	−0.08	−0.03	−0.01	−0.01	−0.14	0.01
Incongruent SDRT	**−0.22***	−0.06	−0.02	0.01	−0.02	**−0.28***	−0.07
Incongruent CVRT	−0.14	0.01	0.00	−0.02	0.00	**−0.25***	−0.08
Neuroelectric outcomes							
Theta power	**0.15***	0.02	−0.03	0.10	−0.12	−0.05	**−0.31***

Bold values denotes significant β (p < .05).

*Significant correlation, p <.05.

TABLE 4 Summary of results of hierarchical regression analyses between cardiorespiratory fitness and behaviral/neuroelectric outcomes

	ΔR^2	ANOVA	B	*SE* B	*β*	*p*	t	95% CI
Behavioral outcomes								
Congruent accuracy[a]	0.03	<0.001	4.23	1.97	**0.16**	0.034	2.14	0.33, 8.11
Incongruent accuracy[a]	0.03	0.002	4.31	1.91	**0.17**	0.025	2.25	0.54, 8.09
Congruent SDRT[a]	0.02	<0.001	−16.62	8.39	**−0.14**	0.049	−1.98	−33.18, −0.06
Congruent CVRT[a]	0.02	0.002	−0.03	0.01	−0.15[†]	0.052	−1.96	−0.05, 0.00
Neuroelectric outcomes								
Theta power[b]	0.09	<0.001	−0.69	0.17	**−0.31**	<0.001	−4.14	−1.02, −0.36

Bold values denotes significant *β* ($p < .05$).

[a]Adjusted for age and IQ in step 1.

[b]Adjusted for age in step 1.

[†]Denotes a trend of p <.01.

be a mediator of the relationship between fitness and flanker task performance.

4 | DISCUSSION

The aim of the current study was to examine the association of childhood cardiorespiratory fitness with midfrontal theta oscillations during an inhibitory control task. Neuroelectric data revealed that higher cardiorespiratory fitness is correlated with smaller midfrontal theta oscillatory power across congruency trials. Such data suggest that greater childhood cardiorespiratory fitness is associated with more favorable modulation of top-down control and cortical communication, as reflected by midfrontal theta. Of note, we verified this association in a large group of children ($n = 171$), providing strong support for the relationship between cardiorespiratory fitness and midfrontal theta oscillation during childhood. Moreover, behavioral data suggest that higher cardiorespiratory fitness is associated with higher response accuracy across congruency trials as well as smaller SDRT and CVRT during trials with lower cognitive demands. Critically, our results did not support midfrontal theta as a mediator of the relationship between higher fitness and task performance on a flanker task, indicating that the positive influence of higher fitness on inhibitory control was not driven by favorable modulation of midfrontal theta associated with higher fitness. However, the relationship between cardiorespiratory fitness and midfrontal theta reported herein provides relevant information in children given the unique role of midfrontal theta in probing typical and atypical development in frontally mediated top-down control.

Consonant with our hypothesis, higher cardiorespiratory fitness was associated with more favorable modulation (i.e., downregulation) in overall midfrontal theta power during tasks with variable amounts of inhibitory control. Midfrontal theta reflects modulations in the frontally mediated top-down control processes, which affords better understanding of neural resources invested during the signaling, monitoring, and control of stimulus-response conflict in favor of subsequent behavioral adaptations (Cavanagh & Frank, 2014). Previous studies investigating midfrontal theta as a biomarker of developmental disorders (e.g., ADHD, ASD) further indicated that greater midfrontal theta oscillation was associated with maladaptive top-down control, where top-down control was overly implemented during task execution and decision making (Kawasaki et al., 2017; Lenartowicz et al., 2014). From a developmental perspective, smaller (or downregulation of) midfrontal theta involvement may be indicative of relatively mature cognitive control in children. Specifically, cognitive control regulation changes across childhood through an increased functional specialization of brain systems that are initially relatively undifferentiated (Johnson & Munakata, 2005), which could be manifested by downregulation in specific brain regions (e.g., frontal cortex, ACC) that underlie cognitive control (Velanova, Wheeler, & Luna, 2008). A recent study in preschoolers and school-aged children has indicated that upreguation in midfrontal theta is involved in the implementation of immature cognitive control to support performance on inhibtion-related tasks (Adam et al., 2020). Accordingly, the current findings imply that children with greater cardiorespiraoty fitness may have a relativley mature and efficient top-down control manifested by favorable modualtion in midfrontal theta. State differently, we found that lower cardiorespiratory fitness could be a neural marker of atypical cognitive development characterizing by excessive midfrontal theta involvement during top-down cognitive control, probably as a result of deviant maturation of frontal cortex and undifferentiated (e.g., over communication between cortices) brain networks subserving inhibitory control.

Interestingly, our findings are supported by findings from a study using the frontal N2 component from an event-related

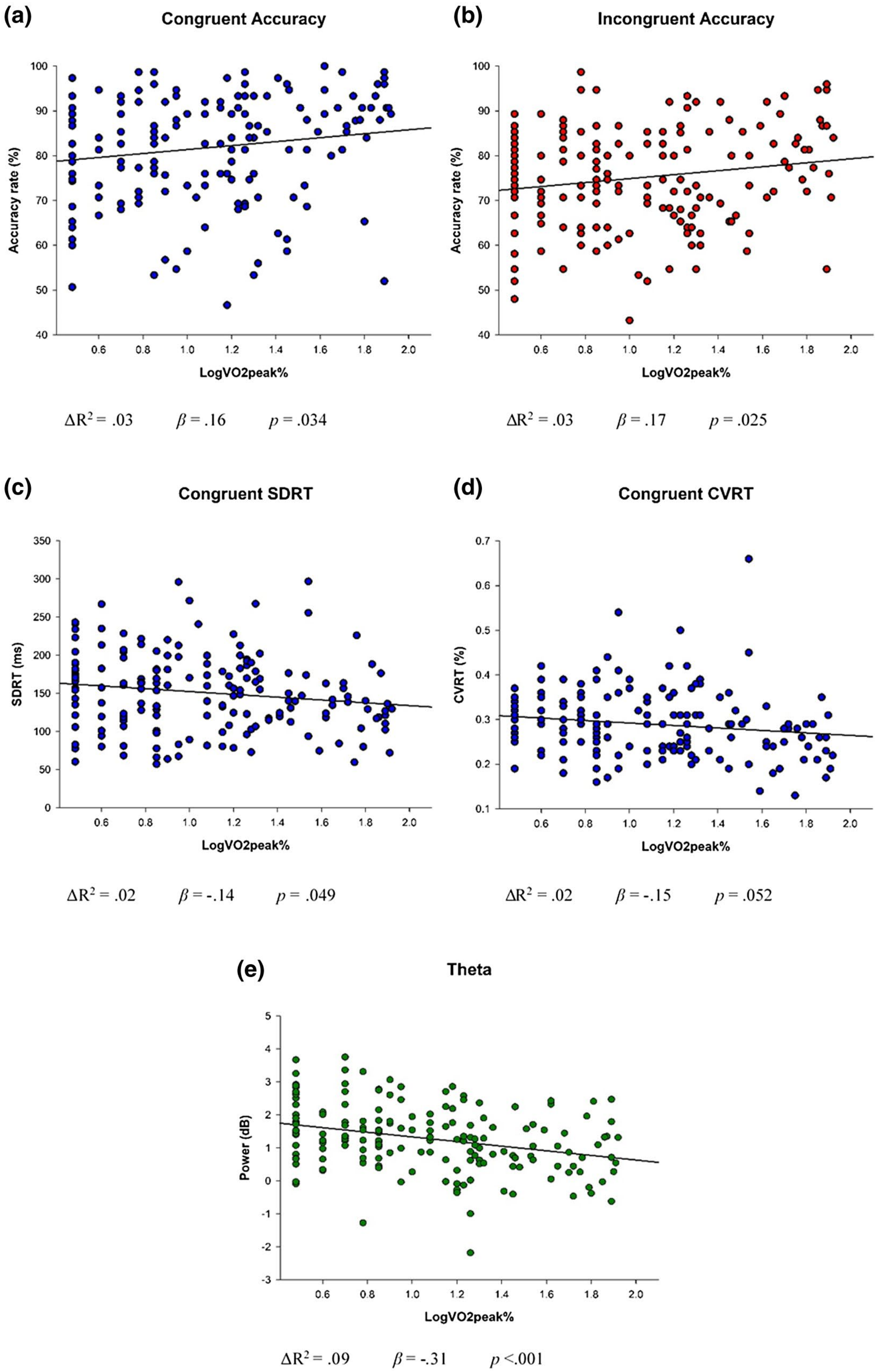

FIGURE 3 Scatter plots depecting associations of cardiorespiratory fitness (i.e., logVO_{2peak}%) with behavioral (i.e., (a) congruent accuracy, (b) incongruent accuracy, (c) congruent SDRT, and (d) congruent CVRT), and (e) overall midfrontal theta power across all 171 participants

brain potential (Pontifex et al., 2011). The frontal N2 is a component elicited between 200 and 400 ms following stimulus onset, which is maximal over the frontocentral scalp region (Larson, Clayson, & Clawson, 2014). The frontal N2 is thought to be specifically related to neural resources required to monitor and detect task-evoked conflicts between stimulus acquisition and response execution (Larson et al., 2014). Specifically, Pontifex et al. (2011) found that lower fit children had larger frontal N2 amplitude, along with worse flanker task performance, relative to higher fit children, suggesting that lower fit children may have experienced more effortful conflict detection and monitoring. However, it is necessary to disambiguate the cognitive implications of frontal N2 from midfrontal theta. For example, rather than simply a neural marker of conflict detection and monitoring such as the frontal N2, midfrontal theta plays an unique role in orchestrating online monitoring and behavioral adaptation by signaling and communicating with long-range task-relevant cortical areas (e.g., lateral prefrontal cortex, motor cortex, parietal cortex and somatosensory cortex) responsible for top-down sensory-motor decision-making, inhibition, and attention modulations when cognitive control is needed (Cavanagh & Frank, 2014; Cohen & Donner, 2013; Duprez et al., 2020).

It is noteworthy that the current study did not find significant congruency effects on midfrontal theta power, which did not align with behavioral data. While the task manipulation effect during a flanker task is robust in adults (Wang et al., 2017), this effect is somewhat ambiguous in children as a previous study has indicated no change in midfrontal theta power despite increased inhibitory control demands (Adam et al., 2020). This could be accounted for, at least in part, by immaturity of the frontal cortex in children and the nature of the inhibitory control tasks. For example, midfrontal theta may be overly implemented in children regardless of task demands, especially under task conditions that are novel and engender uncertainty (Adam et al., 2020). Given that the two congruency trials were randomly presented and our participants only had a relatively short response window (i.e., 1,000 ms), the absence of a task manipulation effect on midfrontal theta may result from the fact that children were not able to flexibly adjust top-down control between congruent and incongruent trials under task conditions with high uncertainty and a short response window. Another alternative is that stimulus-response conflicts embedded within the flanker task were not as strong as other inhibitory control-related tasks such as the Go/No-Go task and stop-signal task. Indeed, recent studies have indicated that task components that strongly focus on response/motor inhibition, such as a Go/No-Go task, may yield stronger task manipulation effects on midfrontal theta modulations than tasks tapping attention inhibition at a perceptual level, such as the flanker task (Nigbur, Ivanova, & Stürmer, 2011). Future study should take this methodological issue into account when addressing the fitness-theta oscillation relationship.

Relative to behavioral outcomes, the data support a positive relationship between increased cardiorespiratory fitness and better performance on a flanker task although such a relationship was not mediated by favorable modulation of midfrontal theta. Although our findings on response accuracy did not observe a larger association of fitness to incongruent trials relative to congruent trials as shown by some studies (Raine et al., 2018), they do align with previous studies indicating higher fitness is associated with superior overall task performance on a flanker task (Berchicci et al., 2015; Pontifex et al., 2011; Wu et al., 2011), implying a generally facilitative effect of increased fitness on performance during tasks with varied amounts of inhibitory control in children. In addition, our data revealed no association between fitness and mean RT. This finding, although contradictory with studies using field-based fitness assessments (e.g., PACER), which found a relationship between greater fitness and shorter mean RT across congruency trials (Scudder et al., 2014: Zhan et al., 2020), is in alignment with research employing gold-standard fitness assessments (i.e., VO_{2peak}) and found a selective relationship of fitness with response accuracy (Berchicci et al., 2015; Pontifex et al., 2011; Raine et al., 2018; Wu et al., 2011). Moreover, our data on SDRT and CVRT indicated that higher fitness is associated with smaller response variability during congruent trials. Notably, intraindividual variability in response speed may be a marker of temporal stability of behavior during task performance (MacDonald, Li, & Bäckman, 2009). Our data showed that, even when mean RT was accounted for, there was still a marginally significant relation between higher fitness and smaller CVRT, suggesting the beneficial effect of increased fitness on behavioral stability during task components with lower cognitive demands. Overall, the current behavioral findings generally support a positive relationship between cardiorespiratory fitness and inhibitory control as assessed by a flanker task in children.

This study is not without limitations that should be acknowledged. First, the cross-sectional design precludes causal inference regarding whether increased cardiorespiratory fitness modulates midfrontal theta oscillations and task performance. Second, the focus of inhibitory control precludes our understanding to other subdomains of cognition (e.g., working memory, cognitive flexibility). Therefore, the current data may not be generalized to other subdomains of cognition. Likewise, the flanker task only measures one aspect of inhibitory control (i.e., attention inhibition), leaving neural oscillations under other aspects of inhibitory control (e.g., motor inhibition) (Diamond, 2013) and their association with fitness unclear. Third, as noted earlier, our participants were comprised of children with relatively low fitness (Supplementary Figure S2), and therefore future study with children from all fitness profiles is needed to have a better picture of the association between childhood fitness and theta oscillations. Lastly, given that there are associations between cognition and childhood physical activity (van Der Niet et al., 2015), more research is warranted to investigate whether physical activity is also associated with midfrontal frontal theta and whether physical activity has confounding/moderating effects on the relationship between cardiorespiratory fitness and midfrontal theta oscillations in children.

In conclusion, the current study indicated that higher cardiorespiratory fitness is associated with smaller overall midfrontal theta oscillatory power. Higher cardiorespiratory fitness is also correlated with better flanker task performance, signified by higher overall response accuracy and greater response consistency during task trials with lower cognitive demands. However, midfrontal theta is unlikely a mediator of the relationship between fitness and flanker task performance, suggesting that the relationship of fitness with midfrontal theta and task performance are independent. Collectively, these findings support the association of increased cardiorespiratory fitness with favorable modulation of top-down control and cortical communication coordinated by midfrontal theta as well as better performance on tasks that vary the amount of inhibitory control during childhood. To the best of our knowledge, the current study is the first to investigate the association of cardiorespiratory fitness with theta oscillations in a large group of children. From a public health perspective, the current data highlight the importance of cardiorespiratory fitness for brain health and cognition during childhood. Future study is recommended to leverage the relationship between higher fitness and smaller midfrontal theta power found herein with typically developing children and in children with developmental disorders.

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CONFLICT OF INTEREST

The authors have indicated they have no potential conflicts of interest to disclose.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

FIGURE S1 Time-frequency plots across all 171 participants
FIGURE S2 Histrogram of VO_{2peak}%

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