Aerobic Exercise, Cognitive Performance, and Brain Activity in Adolescents with Attention-Deficit/Hyperactivity Disorder

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ABSTRACT

VAN RIPER, S. M., G. D. TEMPEST, A. PICCIRILLI, Q. MA, and A. L. REISS. Aerobic Exercise, Cognitive Performance, and Brain Activity in Adolescents with Attention-Deficit/Hyperactivity Disorder. *Med. Sci. Sports Exerc.*, Vol. 55, No. 8, pp. 1445–1455, 2023. **Introduction:** Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder for which behavioral treatments such as exercise are recommended as part of a multidisciplinary treatment program. Exercise improves executive function in individuals with ADHD, but limited information exists regarding the mechanisms involved in the response. We examined task-evoked brain responses during exercise and seated rest in 38 adolescents (n = 15 ADHD; age, 13.6 ± 1.9; male, 73.3%; n = 23 typically developing (TD; age, 13.3 ± 2.1; male, 56.5%)). **Methods:** Participants completed a working memory and inhibitory task while cycling at a moderate intensity for 25 min (i.e., exercise condition) and while seated on the bike without pedaling (i.e., control condition). Conditions were randomized and counterbalanced. Functional near-infrared spectroscopy measured relative changes in oxygenated hemoglobin concentration in 16 brain regions of interest. Brain activity for each cognitive task and condition was examined using linear mixed-effects models with a false discovery rate (FDR) correction. **Results:** The ADHD group had slower response speeds for all tasks and lower response accuracy in the working memory task during exercise compared with the TD group ($P < 0.05$). For the inhibitory task, the ADHD group had lower brain activity in the inferior/superior parietal gyrus during exercise compared with the control condition, whereas the opposite was true for TD ($\mathrm{FDR}_{\mathrm{corrected}}$, $P < 0.05$). For the working memory task, higher brain activity during exercise was observed, regardless of group, in the middle and inferior frontal gyrus and the temporoparietal junction ($\mathrm{FDR}_{\mathrm{corrected}}$, $P < 0.05$). **Conclusions:** Dual-task performance is challenging for adolescents with ADHD, and exercise may modulate neuronal resources in regions such as the temporoparietal junction and frontal areas known to be hypoactive in this population. Future research should examine how these relationships change over time. **Key Words:** FUNCTIONAL NEAR INFRARED SPECTROSCOPY, ADHD, CYCLING, MEMORY, INHIBITION

Attention-deficit/hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder, affecting approximately 6 million children and adolescents in the United States. Diagnosis of ADHD is based on the childhood onset of developmentally inappropriate levels of inattention, hyperactivity, and impulsivity, which are subdomains of a broad category of mental processes termed "executive functions" (1). Executive functions are top-down mental processes needed for decision making, problem solving, and a variety of other cognitive tasks (2). Inhibitory control, which when impaired manifests as inattention, is a core executive function and requires one to control their attention, behavior, thoughts, and/or emotions while overriding external distractors to achieve what is appropriate or needed for a given situation (2). Working memory, another core executive function, has also been observed to be impaired in ADHD and involves holding information in mind and mentally manipulating it (2). Because ADHD is defined by the presence of multiple cognitive impairments, the disorder is significantly heterogeneous in terms of clinical presentation, etiology, and pathophysiology (3–5). Therefore, assessment of multiple domains of executive function is important for comprehensively evaluating ADHD symptomatology.

The complex nature of ADHD has led to development of pharmacological and behavioral treatments for which varying degrees of therapeutic efficacy and adherence have been demonstrated (6). Behavioral interventions are frontline treatments for ADHD and exercise—both acute and chronic—improves executive function and other associated symptoms (7,8). Specifically

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for acute exercise, meta-analytic reviews have consistently reported moderate to large symptom improvements immediately after a single session of moderate-intensity aerobic exercise (65%–75% heart rate (HR) maximum) lasting 20–30 min in duration (7–12). Symptom improvements after exercise have primarily been observed in the executive function domains of inhibitory function, cognitive flexibility, and psychomotor speed, with smaller improvements observed for working memory (7,8,11,12). Cycling and treadmill modalities have typically been used, but there is a significant degree of heterogeneity in terms of study design across all elements of mode, intensity, duration, and executive function outcomes, which has precluded strong conclusions being made regarding the optimal exercise dose to elicit benefit. Meta-analytic evidence also shows that moderate-intensity aerobic exercise training 2–3 times per week for at least 6–12 wk in duration improves executive function domains such as response inhibition, set shifting, and working memory to a moderate to large degree in individuals with ADHD (7–9). Theoretically, the cognitive improvements observed in response to exercise training may represent the cumulative effects observed in the acute response, but this hypothesis has yet to be directly tested (7). The main limitation of this work to date is that the mechanisms underlying the cognitive benefit of exercise have yet to be rigorously interrogated. This knowledge gap has significantly limited our ability to predict responses and provide individualized recommendations to patients.

Functional magnetic resonance imaging (fMRI) studies that measure brain responses to executive function tasks demonstrate that individuals with ADHD display hypoactivity in regions within the frontostriatal, frontoparietal, and ventral attention networks in comparison to population-based controls (13). Investigations incorporating electroencephalography provide evidence that exercise modulates the CNS activity in ADHD (14,15), with support for greater benefit to individuals with lower levels of inhibitory control (16,17). However, the low spatial resolution of electroencephalography and limited ecological validity of fMRI need to be overcame if we are to capture neural function and adaptation in a more translatable manner.

Advances in functional near-infrared spectroscopy (fNIRS) provide new opportunities to probe brain function *during* exercise, which is unobtainable with traditional fMRI. We have previously shown that task-related brain function can be determined *during* moderate-intensity cycling exercise (18). fNIRS is relatively robust to motion artifact and can therefore be applied in less restrictive and more naturalistic settings (19). Using light in the near-infrared spectrum, fNIRS measures changes in oxygenated (HbO) and deoxygenated hemoglobin concentration (HbR) in the cerebral cortex. Cortical activity leads to an increase in oxygen consumption, accompanied by an increase in cerebral blood flow known as neurovascular coupling (20). The changes in HbO and HbR observed in fNIRS have been validated against the blood-oxygen-level–dependent signal of fMRI (21).

Applications of fNIRS to exercise research are increasing, but a majority of studies thus far have examined brain responses before and/or after exercise in healthy young or older adult populations (19). A frequent finding across this literature has been increases in HbO in the prefrontal brain regions after exercise (19), which is particularly relevant considering the hypoactivity observed in individuals with ADHD. Understanding how neuronal circuitry may be modified with exercise in individuals with ADHD will be important for predicting which patients respond best to this type of therapy.

In the current study, we compared task-related brain activity and cognitive performance during moderate-intensity cycling exercise in adolescents with and without ADHD. The purpose of measuring brain activity during exercise is to identify which brain areas/networks are the most susceptible to change in response to an acute bout of exercise. Identification of brain areas/networks that respond acutely will provide foundational mechanistic information about brain biomarkers that could be monitored alongside cognitive performance measures in future longitudinal studies. In this way, we can begin to uncover new insights into brain–behavior relationships that are most important for the exercise responses of individuals with ADHD. Because individuals with ADHD present with hypoactivation of brain areas involved in executive function (e.g., the prefrontal and parietal cortices [13,22]) and because acute exercise often improves executive function, we expected that during cycling exercise, greater improvements in brain function and cognitive performance would be observed in the ADHD group compared with (a) seated rest and (b) a typically developing (TD) group.

METHODS

Participants

Adolescents age 10–18 yr with ADHD (n = 15) or who were TD (n = 23) were recruited from the local community via university mailing lists and campus-wide online advertisements. The parents or guardians completed an online screening form indicating their interest in the study. For the ADHD group, participants were eligible if they had received a diagnosis of ADHD from a qualified health care practitioner (i.e., psychologist, pediatrician psychiatrist). For the ADHD and TD groups, participants were excluded if they had a history of serious medical, neurological, psychiatric illnesses or physical/sensory impairments. Participants with a medical condition precluding participation in physical exercise were also excluded based on the Physical Activity Readiness Questionnaire (23). The majority of participants (95%) reported engaging in PA 3–4 times per week. Participants were invited to the laboratory to go through the study information, and written informed consent and child assent were obtained from their parent/guardian and the participant before participation. In all cases, the parent and child agreed to participate. All participants were unmedicated on the days of testing. The study was approved by Stanford University Institutional Review Board, and the protocol was performed in accordance with the declaration of Helsinki.

Procedures

Participants visited the laboratory on three occasions to complete behavioral assessments, exercise testing, and a nonexercise control session. The order of the exercise and nonexercise sessions was randomized and counterbalanced. For the first visit, participants provided their written informed consent and child assent, and their age, height, and weight were recorded. To confirm the presence of ADHD symptoms, a trained research assistant administered the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version (24) individually to parents/guardians and participants. The participant's IQ was measured using the four-subtest Wechsler Abbreviated Scale of Intelligence—Second Edition (WASI-II [25]). Participants were familiarized with the exercise equipment, which consisted of a bicycle (Sirrus; Specialized Bicycle Components, Morgan Hill, CA) mounted on an indoor trainer (Kickr; Wahoo Fitness, Atlanta, GA [26]). Participants were provided with verbal instructions for how complete the cognitive tasks that assessed two domains of executive function—working memory and inhibitory control—to prepare them for the subsequent sessions.

Participants returned for two remaining sessions: 1) exercise at a moderate intensity in combination with cognitive tasks (exercise condition) or 2) seated rest (a nonexercise control condition) with cognitive tasks. Upon arrival, the participants were fitted with a chest-worn HR monitor (Tickr; Wahoo Fitness) and an fNIRS headcap. Participants were then seated on the exercise bike, and the cognitive task instructions were provided. In the exercise condition, participants began by completing a 5-min warm-up at 40 W. After the warm-up, the wattage was increased to achieve a target intensity of 65% of age-predicted HR maximum (27) equating to moderate-intensity exercise. Once achieved (approximately 3 min), the participants completed the cognitive tasks (approximately 10 min each order counterbalanced) with a short break (30–60 s between trials) during the tasks and a slightly longer break (up to 2 min) between the tasks, while continuously cycling (exercise) or at rest (control). The participants were instructed to maintain a cadence of greater than 60 rpm throughout the exercise protocol (approx. 25 min) and were prompted to speed up if they dropped below 60 rpm. HR was monitored by the experimenter throughout and the wattage adjusted if HR deviated from the target HR ±5 bpm. The participants were otherwise blind to their HR, cadence, and performance measures. Rating of perceived exertion (RPE) using the Borg 6–20 scale (28) was recorded after warm-up, between cognitive tasks, and before the end of exercise. Upon completion of the cognitive tasks and cycling protocol, the participants completed a cool-down at a self-selected intensity for up to 5 min. After completion of the exercise, the fNIRS cap was removed. In the control condition, the participants followed the exact same protocol in regard to the cognitive task except that they did not perform any exercise (i.e., they remained stationary and seated on the bicycle for the warm-up period and administration of the cognitive tasks). As such, counterbalancing, task duration, stimulus timings, and rest periods were identical in the exercise and nonexercise conditions.

Measures

Assessment of working memory. A 0-, 1-, and 2-back visuospatial *n*-back task was used to assess working memory. The *n*-back visuospatial task was originally developed by Kirchner (29) and is a valid and reliable measure of working memory across the life span (30). The *n*-back requires the storage and continual updating of information in working memory as well as interference resolution (31). Functional neuroimaging studies commonly use the *n*-back tasks to identify neuronal mechanisms involved in working memory across a variety of age ranges from children and adolescents (32) to the elderly (33). Meta-analytic evidence has shown that key brain regions involved in working memory, such as the frontal and parietal cortices, are consistently and reliably activated during the *n*-back task (34).

For each *n*-back task block, a circle appeared in 1 of 16 locations on a 15-inch computer screen placed approximately 80 cm in front of the participant's eyeline (on a table above the bike handlebars) for 0.35 s with an intertrial interval of 2 s, during which time the participant could respond. In the 0-back condition, participants responded when the circle appeared in the top right portion of the screen. In the 1-back and 2-back conditions, participants responded when the circle appeared in the same position as one or two trials before, respectively. Responses were recorded by a right thumb button press using an external button box fixed to the right handlebar of the bike. There were five blocks each of the 0-, 1-, and 2-back conditions, presented in a pseudorandom order, each made up of 8–12 trials with 3–4 target trials (requiring a response) per block. Block durations ranged from 18.8 to 28.2 s, depending on the number of trials, with variable interblock intervals of 10–14 s. The number of correct responses (a button press on a target trial) and corresponding response times were recorded.

Assessment of inhibitory control. A Go/NoGo task was used to assess inhibitory control. The Go/NoGo was originally implemented by Gordon and Caramazza (35) and is a continuous performance task that has been demonstrated to be a valid and reliable assessment of response inhibition in children and adults (36). Furthermore, meta-analyses of functional neuroimaging studies involving Go/NoGo to assess response inhibition have consistently demonstrated activation of brain regions involved in attentional control such as the dorsolateral prefrontal cortex and inferior parietal (37). For this task, single letters were presented sequentially in the center of the computer screen for 500 ms, with the distance of the screen and response button in the same location as described previously. The participants were instructed to press a button for any letter other than "X" (go trials; 150 total trials) but not to press when "X" was shown (no-go trials; 50 total trials). Intertrial intervals were variable and ranged between 1 and 10 s, skewed heavily toward shorter intertrial intervals (mean, 2.5 s). Again, we recorded the number of correct responses and response times.

Functional NIRS

An fNIRS system (NIRSport1 Tandem; NIRx, Berlin, Germany) consisting of 16 LED illumination time-multiplexed sources and 16 silicon photodiode detectors was used to measure cortical activity. The optodes transmitted or detected light at two wavelengths (760 and 850 nm) and recorded relative changes in the concentrations of HbO and HbR at a sample rate of 7.8125 Hz. Optodes were secured into plastic holders on a head cap, which was positioned onto the participant's head using landmarks of the 10/20 system for electrode placement applicable to NIRS optode arrangements. The optode holders were positioned 3 cm apart over bilateral prefrontal, temporal, and parietal regions of the cortex, and nearby source—detector pairs made of 42 measurement locations or channels (Fig. 1). The fNIRS system was calibrated before each measurement, and signal quality at the start of the scan was recorded.

Data Analysis

Behavioral responses. To reduce response bias and increase sensitivity, accuracy for the *n*-back and Go/NoGo tasks was expressed as *d* prime (d'). To compute d', the *z* score of the false alarm rate (i.e., commissions) was subtracted from the *z* score of the correct response rate (i.e., hits) (38). This measure is a widely used as a measure of task performance (i.e., signal detection) because it takes into consideration the relative frequency of correct hits and correct rejections (39,40). If participants correctly responded to a high number of targets and correctly withheld a response to a high number of nontargets, then they would have a high d' value (39). Conversely, if the participant responded to a fewer number of targets (omission errors) and/or failed to withhold a response to a larger number of nontargets (commission errors), then they would have a low d' value (39). Mean reaction time (ms) was also assessed to measure processing speed.

Functional NIRS. The fNIRS data processing was performed using the HOMER2 NIRS processing package (41), following guidelines set forth by Brigadoi and colleagues (42). Raw optical data were converted to changes in optical density units. Channels with poor signal quality (defined as a signal-to-noise ratio of less than 3) were excluded from subsequent analyses. To reduce the influence of motion artifacts, we used a hybrid approach described in another high-motion paradigm (43). Optical density data were first conservatively corrected for motion artifacts using spline interpolation followed by an additional step: wavelet filtering (44). All parameters matched those described in Di Lorenzo and colleagues (43). A band-pass filter (0.01–0.5 Hz) was applied to the corrected optical density data, which were converted to HbO and HbR concentrations (in micromolar) using the modified Beer–Lambert equation (41) and differential pathlength factors estimated by age (45).

For both tasks, general linear models were used to estimate the amplitude of each participant's hemodynamic response as a function of stimulus presentation, split by condition (46). We then contrasted the β estimates of the conditions, for example, 2-back–0-back, to isolate the cortical activity that was specific to the task: for *n*-back, the activity related to the degree of difficulty (2-back–0-back, 2-back–1-back), and for Go/NoGo, the activity related to the participant's inhibitory response (NoGo - Go). We then used functional localization (47) to address structural and functional differences in brain anatomy, creating regions of interest (ROIs) by grouping channels together according to their common source. In subsequent analyses, each source ROI is represented by the largest β contrast estimate of its member channels.

Statistical Analysis

Demographics. Demographic (age, height, weight, sex, and WASI-II score) and exercise data (average HR, RPE, cadence, and power) were compared between the ADHD and TD groups using independent Student's *t*-tests or χ^2 tests where appropriate. Effect sizes were estimated using Hedges' *g* for parametric or Cramer's *V* for nonparametric data, respectively (48). The significance level was set to an of $\alpha = 0.05$ for all analyses. SPSS (version 27) was used for all demographic and subsequent analyses.

Behavioral response. To compare response accuracy (d') and mean response time (ms) for the 1- and 2-back working-memory (*n*-back) task and inhibitory control (NoGo/Go) task,

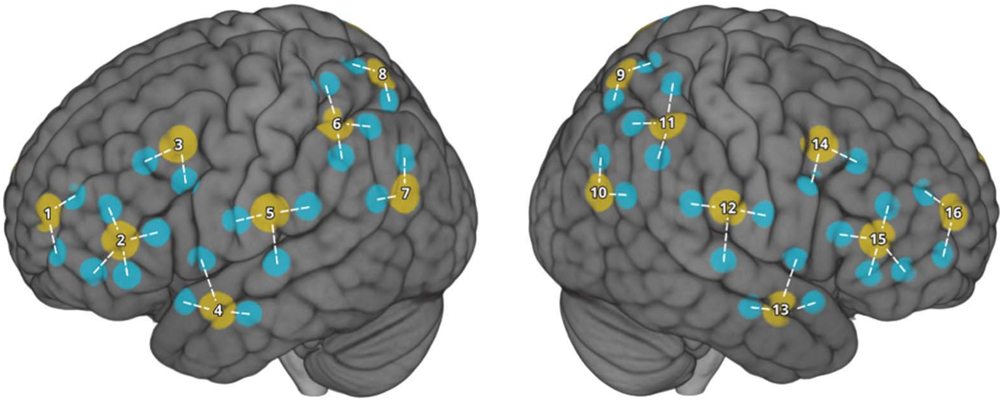

FIGURE 1—Channel array montage. Locations of the source optodes (*yellow circles*) and detector optodes (*blue circles*). Regions of interest were created from channels located over bilateral prefrontal, parietal, and temporal cortices.

TABLE 1. Group comparisons of demographics, physiological, and perceptual responses to exercise.

	ADHD (n = 15), Mean ± SD	TD (n = 23), Mean ± SD	Effect Size	P
Age (yr)	13.6 ± 1.9	13.3 ± 2.1	g = −0.17	0.61
Height (inches)	63.9 ± 4.6	62.9 ± 6.5	g = −0.17	0.61
Weight (lb)	114.0 ± 28.7	114.2 ± 38.2	g = 0.01	0.99
WASI-II score	105.1 ± 14.6	112.7 ± 11.0	g = 0.61	0.08
Sex, % male (n)	73.3 (11)	56.5 (13)	V = 0.17	0.29
ADHD type (K-SADS)	13 inattentive, 2 combined			
Average heart rate (bpm)	131 ± 9	130 ± 13	g = 0.09	0.86
Average RPE	14 ± 2	14 ± 1	g = 0.00	0.9
Average cadence (rpm)	64 ± 9	66 ± 7	g = −0.25	0.46
Average power (W)	65 ± 17	58 ± 25	g = 0.32	0.31

Values are means ± SD unless otherwise noted. Effect sizes are either Hedges' g or Cramer's V. For Hedges' g, 0.2, 0.5, and 0.8 are described as small, medium, and large, respectively. For Cramer's V, 0.1, 0.3, and 0.5 are described as small, medium, and large, respectively (51). K-SADS, Schedule for Affective Disorders and Schizophrenia for School-Age Children.

separate linear mixed models were conducted. Group (ADHD and TD) and condition (exercise and control) served as fixed effects, subject-level intercepts served as random effects. Age was mean centered and used as a covariate of noninterest in all analyses. The covariance matrix type was designated as scaled identity. The maximum likelihood method of estimation, with a Satterthwaite approximation of degrees of freedom, was used for all models. All figures were created in R (version 2021.9.1) using the ggplot2 package. The significance level was set to an of $\alpha = 0.05$ for all behavioral analyses.

Functional NIRS. To compare β estimates for task-related changes in HbO, separate linear mixed models were conducted for each of 16 source ROIs. Group (ADHD and TD) and condition (exercise and control) served as fixed effects, and within the same subject, repeated measurements for both conditions were assumed to be correlated. The repeated covariance matrix type was designated as compound symmetry—heterogeneous. Age was mean centered and used as a covariate of noninterest in all analyses because of its established relationship to both cognitive function and brain activity (49). The maximum likelihood method of estimation, with a Satterthwaite approximation of degrees of freedom, was used for all models. False discovery rate (FDR [50]) was used to correct for multiple comparison for the 16 ROIs conducted for each contrast (i.e., Go/NoGo, 2–0 back, 2–1 back). The significance level was set to an α of 0.05 for all functional analyses, and only significant main or interaction effects are reported.

Exploratory Analyses: Associations between Behavioral and fNIRS Responses

ROIs with significant main and/or interaction effects uncovered in our primary analyses were further explored by examining the relationships between brain activity and cognitive performance separately for each group and condition. To achieve this, Spearman's correlations were conducted using HbO, mean reaction time, and response accuracy (d') (uncorrected, $P < 0.05$).

RESULTS

Demographics

Demographics and IQ measurements at baseline are presented in Table 1. Groups (ADHD vs TD) were not significantly different on age, height, weight, IQ, or sex.

Exercise Responses

Exercise performance data and perceptual ratings are presented in Table 1. Groups did not significantly differ on HR, RPE, power output, or cadence.

Behavioral Responses

Response data for the cognitive tasks performed during exercise and control conditions are presented in Table 2. Across tasks, lower response accuracy was observed in the ADHD group during exercise for the completion of the 1-back working memory task, whereas reaction time impairments were observed in the ADHD group across all three cognitive tasks (i.e., Go/NoGo, 2-back, 1-back). These findings are further described in subsequent sections hereinafter.

TABLE 2. Group comparisons of cognitive task performance.

		ADHD (n = 15)		TD (n = 21)		
Task	Outcome	Control, Mean ± SD	Exercise, Mean ± SD	Control, Mean ± SD	Exercise, Mean ± SD	Effect Size
Go/NoGo	d'	2.02 ± 0.69	1.77 ± 0.63	2.41 ± 0.98	2.07 ± 0.60	g = 0.10
	Mean RT (ms)	0.52 ± 0.05	0.51 ± 0.05	0.49 ± 0.04	0.48 ± 0.05	g = 0.00
	Hits	139.5 ± 8.35	133.7 ± 15.10	134.3 ± 31.99	133.5 ± 31.35	g = −0.20
	False alarms	16.4 ± 8.80	17.3 ± 7.86	13.1 ± 7.75	15.8 ± 9.25	g = −0.22
2-Back	d'	2.40 ± 0.79	1.86 ± 0.91	2.58 ± 1.08	2.32 ± 0.95	g = −0.29
	Mean RT (ms)	0.71 ± 0.16	0.70 ± 0.18	0.59 ± 0.08	0.59 ± 0.17	g = −0.08
	Hits	11.5 ± 2.47	10.3 ± 3.15	12 ± 4.02	11 ± 3.77	g = −0.06
	False alarms	2.2 ± 2.51	3 ± 2.78	1.5 ± 2.39	1.5 ± 1.83	g = 0.33
1-Back	d'	2.75 ± 1.26	2.54 ± 1.11	2.77 ± 0.90	2.93 ± 1.10	g = −0.35
	Mean RT (ms)	0.67 ± 0.13	0.64 ± 0.11	0.59 ± 0.11	0.54 ± 0.13	g = 0.17
	Hits	13.3 ± 3.60	12.7 ± 3.87	12.9 ± 3.78	13.2 ± 3.88	g = −0.24
	False alarms	2.3 ± 3.09	2.3 ± 2.43	1.3 ± 1.29	1.2 ± 1.41	g = 0.05

Values are means ± SD. Effect sizes are Hedges' g and represent the interaction between groups and conditions such that ($g = \{[(\text{Mean}_{\text{Exercise(ADHD)}} - \text{Mean}_{\text{Control(ADHD)}})/\text{SD}_{\text{control(ADHD)}}] - [(\text{Mean}_{\text{Exercise(TD)}} - \text{Mean}_{\text{Control(TD)}})/\text{SD}_{\text{control(TD)}}]/\text{SDpooled}\}$. For Hedges' g, 0.2, 0.5, and 0.8 are described as small, medium, and large, respectively. Higher mean reaction time (ms) is indicative of slower responses, whereas higher d' values indicate higher response accuracy (i.e., sensitivity). Values for hits represent the number correct responses and false alarm values represent the errors of commission.
RT = reaction time.

Go/NoGo—Inhibitory Control Task

Response accuracy (*d*′). No main or interaction effects were observed for response accuracy (*d*′: $P > 0.05$).

Reaction time (ms). A significant main effect of group revealed higher mean reaction time, indicative of slower responses, for the ADHD group compared with the TD group ($F(1,67) = 4.79$, $P = 0.032$; Fig. 2A).

2-Back—Working-Memory Task

Response accuracy (*d*′). No main or interaction effects were observed for response accuracy (*d*′: $P > 0.05$).

Reaction time (ms). A significant main effect of group revealed higher mean reaction time, indicative of slower responses, for the ADHD group compared with the TD group ($F(1,72) = 7.57$, $P = 0.008$; Fig. 2B).

1-Back—Working-Memory Task

Response accuracy (*d*′). A group–condition interaction was observed for response accuracy (*d*′: $F(1,37) = 4.25$, $P = 0.046$). The ADHD group had lower response accuracy during exercise compared with the control, whereas the TD group had higher response accuracy during exercise compared with control (Fig. 2C).

Reaction time (ms). A significant main effect of group revealed higher mean reaction time, indicative of slower responses, for the ADHD group compared with the TD group ($F(1,58) = 6.40$, $P = 0.014$; Fig. 2D).

Brain Activity Measures with fNIRS

Brain activity during the Go/NoGo inhibitory control task. For inhibitory (Go/NoGo) task-evoked brain activity, a group–condition interaction was observed for the ROI encompassing the inferior and superior parietal gyrus (source 6, $F(1,34) = 14.48$, FDR$_{\text{corrected}}$ $P = 0.001$; Fig. 3). The ADHD group had lower brain activity during exercise compared with the control condition, whereas the opposite was true for the TD group. A main effect of group was observed, such that higher brain activity occurred in this region for the ADHD group compared with the TD group ($F(1,36) = 20.2$, FDR$_{\text{corrected}}$ $P = 0.000071$; see Supplemental Table 1, Supplemental Digital Content, which presents the ROIs that did not survive multiple comparison correction, http://links.lww.com/MSS/C824).

Brain activity during the N-back working memory task. For the 2–0 back contrast, a main effect of condition showed higher task-evoked brain activity during exercise for the ROI encompassing the middle and inferior frontal gyrus (source 2, $F(1,39) = 12.69$, FDR$_{\text{corrected}}$ $P = 0.001$; Fig. 4). A group main effect and group–condition interaction effect were

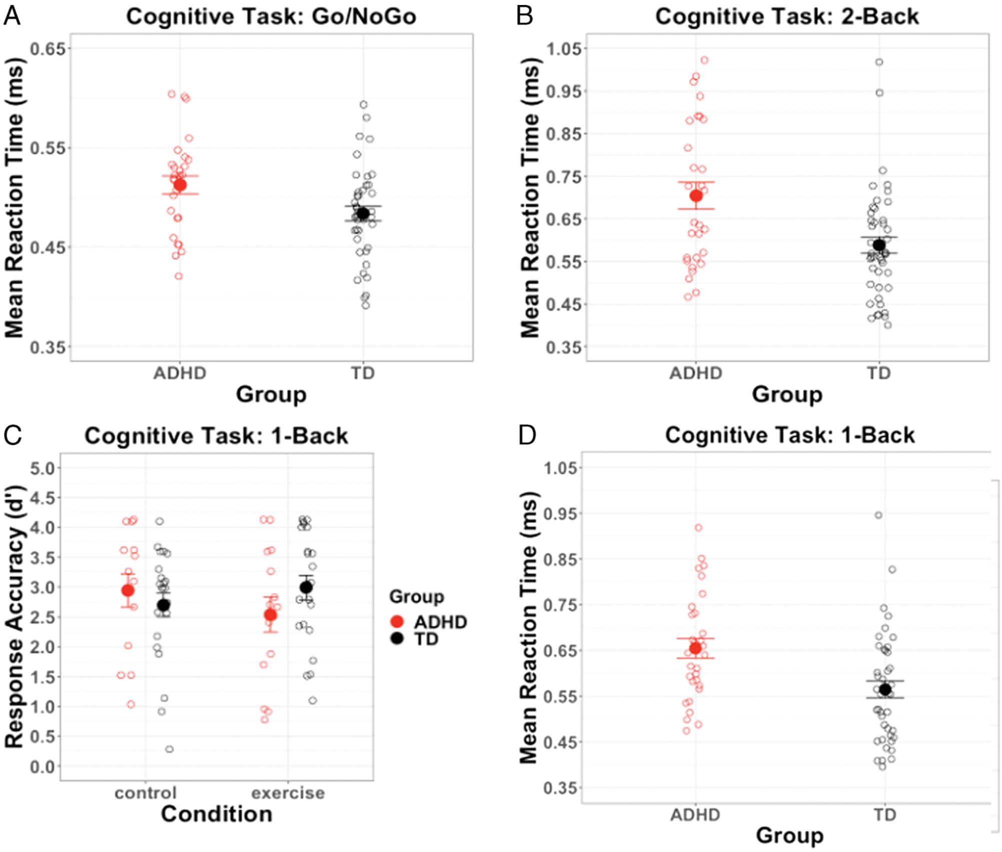

FIGURE 2—Differences in reaction time and response accuracy during the behavioral tasks. Average reaction time and response accuracy, with SEM, for the Go/NoGo inhibitory and *n*-back task. Higher mean reaction time indicates slower response speed. Higher values of *d*′ indicate better response accuracy.

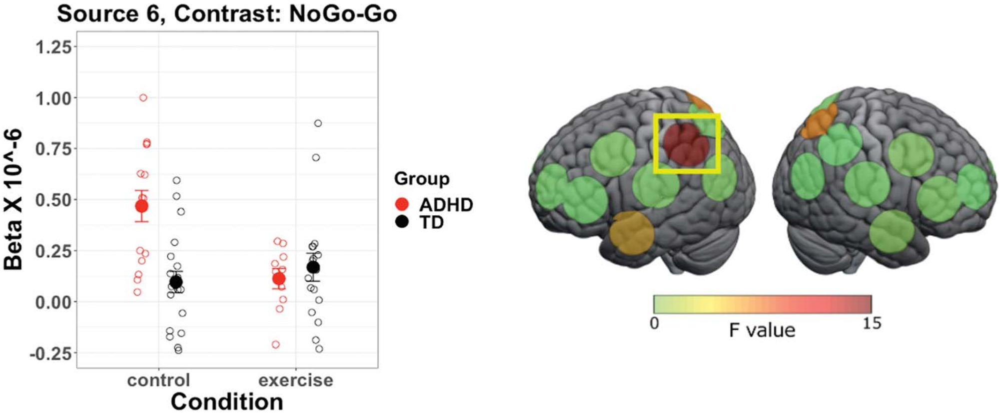

FIGURE 3—Inhibitory task–evoked brain activity in the parietal cortex. Average cortical activation (HbO), with SEM, by group and condition for the Go/NoGo contrast in source 6, which encompasses the inferior and superior parietal gyrus ($F(1,34) = 14.48$, FDR$_{\text{corrected}}$ $P = 0.001$).

also observed in this region, but these effects did not survive multiple comparison correction (see Supplemental Table 2, Supplemental Digital Content, which presents ROIs that did not survive multiple comparison correction, http://links.lww.com/MSS/C824).

For the 2–1 back contrast, a main effect of condition showed higher task-evoked brain activity during exercise for the ROI encompassing the junction of the postcentral, inferior parietal, and superior temporal gyrus (Source 5, $F(1,39) = 10.78$, FDR$_{\text{corrected}}$ $P = 0.002$; Fig. 5). For additional ROIs that did not survive multiple comparison correction, see Supplemental Table 3, Supplemental Digital Content, http://links.lww.com/MSS/C824.

Associations between Behavioral Responses and Brain Activity

Go/NoGo inhibitory control task. A significant positive association was observed between brain activity and mean reaction time for the ROI encompassing the inferior and superior parietal gyrus for the TD group during the control condition (source 6, $r = 0.690$, $P_{\text{uncorrected}} = 0.001$; Fig. 6).

***N*-back working memory task.** No significant associations were observed for the brain activity of source 2 and cognitive performance on the 2–0 back task. A significant negative association was observed between brain activity and 2–1 back response accuracy (*d′*) for the ROI encompassing the junction of the postcentral, inferior parietal, and superior temporal gyrus for the TD group during exercise (source 5, $r = -0.452$, $P_{\text{uncorrected}} = 0.041$).

DISCUSSION

The overall goal of this study was to determine the effect of moderate-intensity cycling exercise on *concurrent* cognitive function and corresponding task-based brain activity in individuals with and without ADHD. As planned, groups did not differ on key demographic variables and performance on the exercise. Main and interaction effects were observed for cognitive task performance and brain activity. Interpretation of the findings is detailed hereinafter.

Inhibitory and working memory function during exercise and control. Across the inhibitory and working memory tasks, the ADHD group showed higher mean reaction times, indicative of slower processing speeds, compared with the TD group regardless of condition. Impairments in response inhibition and working memory are consistent deficits observed in this population, with meta-analyses reporting moderate

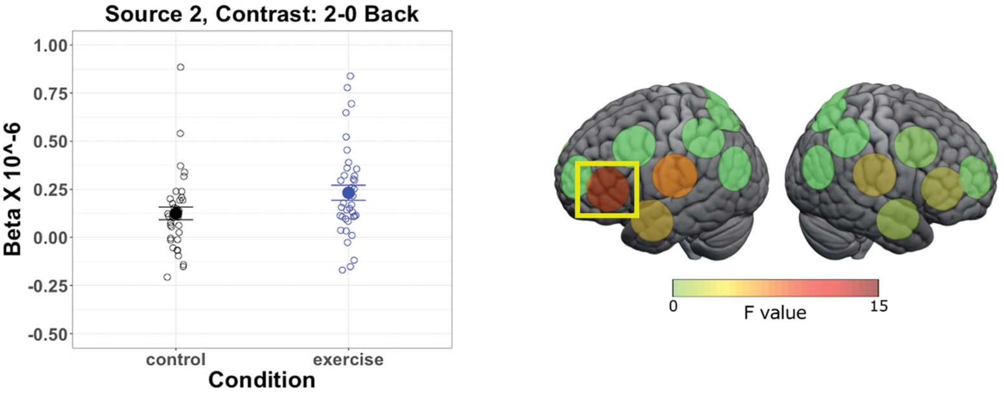

FIGURE 4—Working memory task–evoked brain activity in the middle and inferior frontal gyrus. Average cortical activation (HbO), with SEM, by condition for the 2–0 contrast in source 2, which encompasses middle and inferior frontal gyrus ($F(1,39) = 12.69$, FDR$_{\text{corrected}}$ $P = 0.001$).

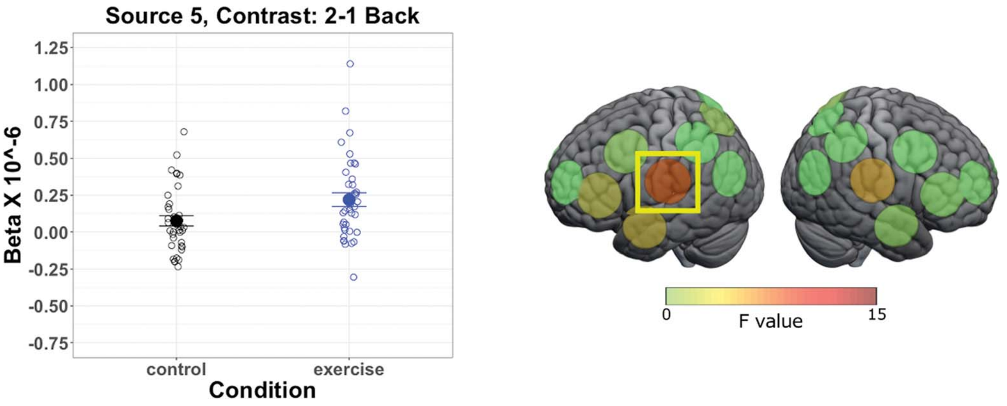

FIGURE 5—Working memory task–evoked brain activity in the middle and inferior frontal gyrus. Average cortical activation (HbO), with SEM, by condition for the 2–1 contrast in source 2, which encompasses the junction of the postcentral, inferior parietal, and superior temporal gyrus ($F(1,39) = 10.78$, $\mathrm{FDR}_{\mathrm{corrected}}$ $P = 0.001$).

differences between individuals with ADHD and controls (52). Slower processing speeds have been observed across multiple executive function domains in individuals with ADHD, which may negatively impact the rate of learning, retrieval of information, and problem solving, and may also play a role in mental fatigue (53,54).

A group–condition interaction was observed for response accuracy during the 1-back working memory task. The ADHD group had lower response accuracy for the 1-back task during exercise compared with the control condition and the TD group. For this study design, exercise and the cognitive tasks were performed concurrently. Therefore, the lower response accuracy (1-back) of the ADHD group during exercise highlights how cognitive impairment could be amplified when children with this condition are required to perform tasks involving both a mental and physical load. The observed interaction also suggests that cognitive function improved during exercise in TD individuals. Given that the ADHD and TD groups were not different in terms of maintenance of target HR throughout the exercise, it seems that the dual-task design used here led to more decrement in response speed and select aspects of response accuracy (i.e., 1-back) in the ADHD group and improvement in accuracy for the TD group.

The 2-back task was expected to be more difficult in comparison to the 1-back task for response accuracy (and reaction time), and this pattern (1-back vs 2-back) can be observed in Table 2. However, the main finding of similar response accuracy across groups and conditions for the 2-back suggests that increasing task difficulty in conjunction with cycling did not result in greater performance deficits. One possible explanation for this lack of consistency between *n*-back versions may be that the combination of a mental and physical load at a higher level of task difficulty resulted in a performance ceiling effect for both groups.

There is limited literature to date examining dual-task performance in individuals with ADHD. In a similar study comparing performance on an auditory attention test while walking or sitting, Rassovsky and Alfassi (55) observed poorer response accuracy during walking in adults with ADHD versus control participants. However, this previous study's results varied depending on the measure of task performance. Using a dual task of varying visual and balance conditions, Caldani et al. (56) found that children with ADHD had poor fixation capability and poor postural stability compared with TD children that varied with task difficulty. Conversely, Shorer et al. (57) reported improvements in postural sway when performed in conjunction with an auditory working memory task for both the ADHD and control groups. Lastly, Manicolo et al. (58) reported that children with ADHD had similar gait performance compared with controls while concurrently performing a cognitive task. These examples demonstrate that the interactive

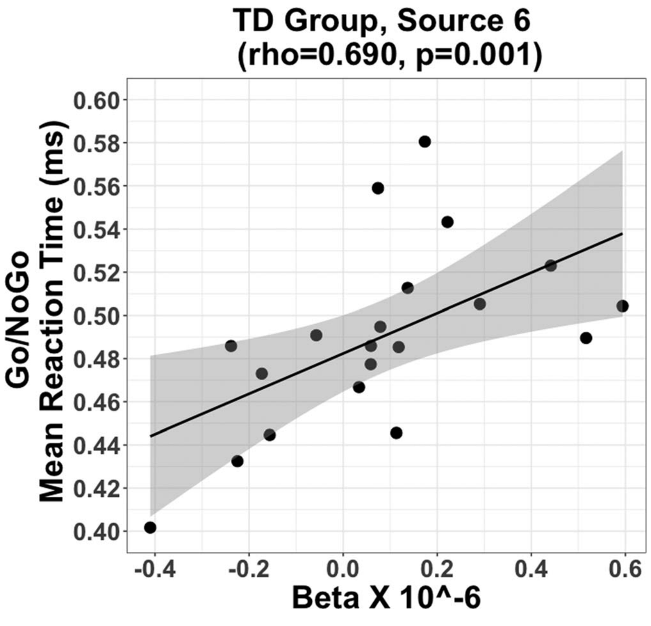

FIGURE 6—Relationship between brain activity and mean reaction time for the Go/NoGo task. Relationship between brain activity (HbO) and mean reaction time during the Go/NoGo inhibitory task for the TD group in source 6, which encompasses the inferior and superior parietal gyrus. Shaded region represents 95% confidence interval. One subject in this analysis was identified as an extreme outlier (defined as >2 SD) and removed for visual clarity. Results remained unchanged with and without this data point.

effects of cognitive and motor task performance seem to be highly variable and dependent on the population studied (e.g., adult vs children, ADHD vs typical developing), choice of attentional, task and corresponding summary of performance measures, as well as the intensity, duration, and type of exercise. The large degree of heterogeneity across this behavioral body of literature precludes our ability to directly compare findings across studies. However, this lack of consistency also demonstrates the need for inclusion of mechanistic outcomes in future work, so that regardless of cognitive task (or other study parameters), the underlying mechanisms that control executive function as a research domain can better be compared (59).

Inhibitory and working memory task–evoked brain activity in response to exercise. Inhibitory task-evoked brain activity in the left junction of the inferior and superior parietal gyrus was found to be differentially affected by exercise. Specifically, brain activity was lower during exercise compared with control for the ADHD group, whereas slightly higher brain activity was observed during exercise (compared with control) for the TD group. This finding is interesting given that behaviorally, no differences in inhibitory task performance were observed between exercise and control, although the ADHD group had slower response times compared with the TD group. The parietal region is a key area involved in top-down attentional control (60). The dorsal frontoparietal network (i.e., lateral frontal cortex, anterior and posterior intraparietal cortex) has been shown to mediate voluntary, sustained orientating of attention, and the ventral attention network (i.e., anterior insula, anterior cingulate cortex, and temporoparietal junction (TPJ)) has been associated with reorienting attention to unexpected or salient stimuli (4,61). Case–control fMRI studies using inhibitory control, working memory, and attentional tasks have shown hypoactivity in brain areas of both the dorsal and ventral attention networks in individuals with ADHD (4). Because brain activity during exercise for the ADHD group became more similar to that of the TD group (Fig. 3), we can infer a shift toward more normative allocation of neuronal resources in this region. This inference is supported by the observation that lower brain activity in this region was associated with faster reaction times for the TD group during the control condition (Fig. 6). It may also be possible that this single exercise dose was not robust enough to improve cognitive performance in tandem with physical exertion.

Working memory task–evoked brain activity in the left middle and inferior frontal gyrus was found to be higher during exercise compared with control for both groups. A similar effect was also observed in a region encompassing the left postcentral, inferior parietal, and superior temporal gyrus (i.e., TPJ). The frontal cortex is a brain region known for its control of higher-order executive functions, including working memory and attentional control, and subregions such as the dorsolateral prefrontal cortex have also been shown to be hypoactive in individuals with ADHD (4,13,62). The TPJ is a region involved in integration of multiple information processing streams. Working memory is a part of TPJ function through its connections to the prefrontal cortex (63,64). Although the left TPJ has been implicated most for language processing, it has also been shown to play a role in a variety of cognitive processes such as decision making (65), social recognition (66), and the Theory of Mind (67). The prefrontal region has been most often shown to increase activity in response to exercise regardless of age or disease state (7,68), with some reports of increases in the parietal regions as well (32).

Exercise training trials in individuals with ADHD consistently show moderate to large improvements in cognitive function (69). However, little information is available regarding how acute brain activity responses to exercise may translate to improvements in cognition found in response to exercise training. In the current study, the novel use of measuring brain activity and cognitive function concurrently during exercise provides foundational information establishing the inferior/middle frontal gyrus, inferior/superior parietal, and superior temporal gyrus as regions most likely to change in response to exercise training. Future randomized controlled trials should measure brain activity in the prefrontal and parietal regions to more fully elucidate how modifications within this network may translate to the postexercise training benefits in cognition most often seen in previous literature (7–9).

Limitations. Although our dual-task paradigm yielded significant results, it is important to point out certain limitations regarding our small sample size that resulted in less than ideal statistical power. The statistical power for testing the interaction between group and condition peaked at 0.70 across 16 ROIs across each of the 3 tasks (i.e., 1-back, 2-back, Go/NoGo). As a result, we were unable to test for the influence of other covariates (besides age, which was planned) such as sex, IQ, physical activity behavior, or others. However, it is important to point out that in comparison to sample sizes reported in recent meta-analyses (i.e., 10–35 participants tested per group), our sample of 38 (15 ADHD, 23 TD) is well within the range of the majority of other reports (7–9). Furthermore, a recent study by Szucs and Ioannidis (70) reported that "96% of highly cited clinical fMRI studies (with patient participants) had median sample size of 14–15."

Other considerations related to our demographic information should also be noted. Our sample of adolescents with ADHD primarily comprised male participants with the inattentive subtype. Although our sample represents the typical 3–4:1 male-to-female ratio reported in epidemiologic studies (1), our results are unable to be generalized to female participants and other ADHD subtypes. Participants were unmedicated at the time of testing; therefore, the influence of stimulant medication was unable to able to be assessed. The participants in this study reported being generally physically active. It is expected that the findings would be more pronounced in individuals who are less active. Socioeconomic status was not recorded as part of this study; therefore, is it unknown how this variable may influence the reported outcomes.

Short-separation channels, which measure extracerebral blood flow, were not available for this study. Inclusion of short-channel data improves signal to noise and may improve the ability to detect differences in brain activity during exercise.

CONCLUSIONS

Using a dual-task paradigm, we demonstrated that adolescents with ADHD were able to successfully achieve the desired moderate-intensity exercise target but were slower in their ability to perform both the inhibitory and working memory task, as well as less accurate for select versions of the *n*-back task (i.e., 1-back). The resulting interaction observed on the 1-back tasks also suggests that TD adolescents improved response accuracy during exercise. Task-evoked brain activity in response to the exercise was altered in regions encompassing select areas of the frontal, parietal, and temporal cortices. These findings suggest that performance of physical and mental tasks in concert is challenging for adolescents with ADHD, but also that exercise may have the potential to modulate neuronal resources in key regions such as the TPJ and frontal areas that are known to be hypoactive in this population. Future research should examine how relationships between cognitive function and brain activity, specifically in the TPJ, inferior and superior parietal, and middle and inferior frontal cortices, change over time. Comparison of dose–response relationships between different exercise intensities and/or durations to both cognitive and brain outcomes is also lacking and will be an important area to expand upon in the future. Information regarding the adaptability of neuronal circuitry to exercise training and its association with cognitive performance will ultimately help to determine which patients or subgroups of patients may respond best to specific doses of exercise.

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The authors have no conflicts of interest to declare. The results of the study do not constitute endorsement by the American College of Sports Medicine. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

REFERENCES

1. Thapar A, Cooper M. Attention deficit hyperactivity disorder. *Lancet*. 2016;387(10024):1240–50.
2. Diamond A. Executive functions. *Annu Rev Psychol*. 2013;64:135–68.
3. Danielson ML, Bitsko RH, Ghandour RM, Holbrook JR, Kogan MD, Blumberg SJ. Prevalence of parent-reported ADHD diagnosis and associated treatment among U.S. children and adolescents, 2016. *J Clin Child Adolesc Psychol*. 2018;47(2):199–212.
4. Faraone SV, Asherson P, Banaschewski T, et al. Attention-deficit/hyperactivity disorder. *Nat Rev Dis Primers*. 2015;1:15020.
5. Wolfers T, Beckmann CF, Hoogman M, Buitelaar JK, Franke B, Marquand AF. Individual differences v. the average patient: mapping the heterogeneity in ADHD using normative models. *Psychol Med*. 2020;50(2):314–23.
6. Corkum P, Bessey M, McGonnell M, Dorbeck A. Barriers to evidence-based treatment for children with attention-deficit/hyperactivity disorder. *Atten Defic Hyperact Disord*. 2015;7(1):49–74.
7. Christiansen L, Beck MM, Bilenberg N, Wienecke J, Astrup A, Lundbye-Jensen J. Effects of exercise on cognitive performance in children and adolescents with ADHD: potential mechanisms and evidence-based recommendations. *J Clin Med*. 2019;8(6):841.
8. Liang X, Li R, Wong SHS, Sum RKW, Sit CHP. The impact of exercise interventions concerning executive functions of children and adolescents with attention-deficit/hyperactive disorder: a systematic review and meta-analysis. *Int J Behav Nutr Phys Act*. 2021;18(1):68.
9. Welsch L, Alliott O, Kelly P, Fawkner S, Booth J, Niven A. The effect of physical activity interventions on executive functions in children with ADHD: a systematic review and meta-analysis. *Ment Health Phys Act*. 2021;20(2):100379.
10. Zang Y. Impact of physical exercise on children with attention deficit hyperactivity disorders: evidence through a meta-analysis. *Medicine (Baltimore)*. 2019;98(46):e17980.
11. Neudecker C, Mewes N, Reimers AK, Woll A. Exercise interventions in children and adolescents with ADHD: a systematic review. *J Atten Disord*. 2019;23(4):307–24.
12. Den Heijer AE, Groen Y, Tucha L, et al. Sweat it out? The effects of physical exercise on cognition and behavior in children and adults with ADHD: a systematic literature review. *J Neural Transm*. 2017;124(1):3–26.
13. Gossé LK, Bell SW, Hosseini SMH. Functional near-infrared spectroscopy in developmental psychiatry: a review of attention deficit hyperactivity disorder. *Eur Arch Psychiatry Clin Neurosci*. 2022;272(2):273–90.
14. Chuang LY, Tsai YJ, Chang YK, Huang CJ, Hung TM. Effects of acute aerobic exercise on response preparation in a Go/No Go Task in children with ADHD: an ERP study. *J Sport Health Sci*. 2015;4(1):82–8.
15. Lee SK, Song JE, Park JH. Effects of combination exercises on electroencephalography and frontal lobe executive function measures in children with ADHD: a pilot study. *Biomed Res*. 2017. Available from: https://www.semanticscholar.org/paper/Effects-of-combination-exercises-on-and-frontal-in-Lee-Song/1679d0ac59767b1702c96c779473ccb0ed6384da. Accessed February 2, 2022.
16. Pontifex MB, Saliba BJ, Raine LB, Picchietti DL, Hillman CH. Exercise improves behavioral, neurocognitive, and scholastic performance in children with attention-deficit/hyperactivity disorder. *J Pediatr*. 2013;162(3):543–51.
17. Drollette ES, Scudder MR, Raine LB, et al. Acute exercise facilitates brain function and cognition in children who need it most: an ERP study of individual differences in inhibitory control capacity. *Dev Cogn Neurosci*. 2014;7:53–64.
18. Tempest GD, Reiss AL. The utility of functional near-infrared spectroscopy for measuring cortical activity during cycling exercise. *Med Sci Sports Exerc*. 2019;51(5):979–87.
19. Herold F, Wiegel P, Scholkmann F, Müller NG. Applications of functional near-infrared spectroscopy (fNIRS) neuroimaging in exercise–cognition science: a systematic, methodology-focused review. *J Clin Med*. 2018;7(12):466.
20. Menon V, Crottaz-Herbette S. Combined EEG and fMRI studies of human brain function. *Int Rev Neurobiol*. 2005;66:291–321.
21. Cui X, Bray S, Bryant DM, Glover GH, Reiss AL. A quantitative comparison of NIRS and fMRI across multiple cognitive tasks. *Neuroimage*. 2011;54(4):2808–21.
22. Cortese S, Kelly C, Chabernaud C, et al. Toward systems neuroscience of ADHD: a meta-analysis of 55 fMRI studies. *Am J Psychiatry*. 2012;169(10):1038–55.
23. Bredin SSD, Gledhill N, Jamnik VK, Warburton DER. PAR-Q+ and ePARmed-X+. *Can Fam Physician*. 2013;59(3):273–7.
24. Kaufman J, Birmaher B, Brent D, et al. Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. *J Am Acad Child Adolesc Psychiatry*. 1997;36(7):980–8.
25. Wechsler D. *Wechsler Abbreviated Scale of Intelligence Second Edition (WASI-II)*. San Antonio, TX: Pearson; 2011.

26. Hoon MW, Michael SW, Patton RL, Chapman PG, Areta JL. A comparison of the accuracy and reliability of the Wahoo KICKR and SRM power meter. *J Sci Cycl*. 2016;5(3):11–5.
27. Tanaka H, Monahan KD, Seals DR. Age-predicted maximal heart rate revisited. *J Am Coll Cardiol*. 2001;37(1):153–6.
28. Borg G. *Borg's Perceived Exertion and Pain Scales*. Champaign (IL): Human Kinetics; 1998. viii, 104 p.
29. Kirchner WK. Age differences in short-term retention of rapidly changing information. *J Exp Psychol*. 1958;55(4):352–8.
30. Schmiedek F, Lövdén M, Lindenberger U. A task is a task is a task: putting complex span, n-back, and other working memory indicators in psychometric context. *Front Psychol*. 2014;5:1475.
31. Sweet LH. N-back paradigm. In: Kreutzer JS, DeLuca J, Caplan B, editors. *Encyclopedia of Clinical Neuropsychology*. New York (NY): Springer; 2011. p. 1718–9.
32. Chen A-G, Zhu L-N, Yan J, Yin H-C. Neural basis of working memory enhancement after acute aerobic exercise: fMRI study of preadolescent children. *Front Psychol*. 2016;7:1804.
33. Yaple ZA, Stevens WD, Arsalidou M. Meta-analyses of the n-back working memory task: fMRI evidence of age-related changes in prefrontal cortex involvement across the adult lifespan. *Neuroimage*. 2019;196:16–31.
34. Wang H, He W, Wu J, Zhang J, Jin Z, Li L. A coordinate-based meta-analysis of the n-back working memory paradigm using activation likelihood estimation. *Brain Cogn*. 2019;132:1–12.
35. Gordon B, Caramazza A. Lexical decision for open- and closed-class words: failure to replicate differential frequency sensitivity. *Brain Lang*. 1982;15(1):143–60.
36. Votruba KL, Langenecker SA. Factor structure, construct validity, and age- and education-based normative data for the Parametric Go/No-Go test. *J Clin Exp Neuropsychol*. 2013;35(2):132–46.
37. Simmonds DJ, Pekar JJ, Mostofsky SH. Meta-analysis of Go/No-Go tasks demonstrating that fMRI activation associated with response inhibition is task-dependent. *Neuropsychologia*. 2008;46(1):224–32.
38. Hautus MJ. Corrections for extreme proportions and their biasing effects on estimated values of *d′*. *Behav Res Methods Instrum Comput*. 1995;27(1):46–51.
39. Foland-Ross LC, Tong G, Mauras N, et al. Brain function differences in children with type 1 diabetes: a functional MRI study of working memory. *Diabetes*. 2020;69(8):1770–8.
40. Haatveit BC, Sundet K, Hugdahl K, Ueland T, Melle I, Andreassen OA. The validity of d prime as a working memory index: results from the "Bergen n-back task." *J Clin Exp Neuropsychol*. 2010;32(8):871–80.
41. Huppert TJ, Diamond SG, Franceschini MA, Boas DA. HomER: a review of time-series analysis methods for near-infrared spectroscopy of the brain. *Appl Optics*. 2009;48(10):D280–98.
42. Brigadoi S, Ceccherini L, Cutini S, et al. Motion artifacts in functional near-infrared spectroscopy: a comparison of motion correction techniques applied to real cognitive data. *Neuroimage*. 2014;85(Pt 1 (0 1)):181–91.
43. Di Lorenzo R, Pirazzoli L, Blasi A, et al. Recommendations for motion correction of infant fNIRS data applicable to multiple data sets and acquisition systems. *Neuroimage*. 2019;200:511–27.
44. Molavi B, Dumont GA. Wavelet-based motion artifact removal for functional near-infrared spectroscopy. *Physiol Meas*. 2012;33(2):259–70.
45. Scholkmann F, Wolf M. General equation for the differential pathlength factor of the frontal human head depending on wavelength and age. *J Biomed Opt*. 2013;18(10):105004.
46. Ye JC, Tak S, Jang KE, Jung J, Jang J. NIRS-SPM: statistical parametric mapping for near-infrared spectroscopy. *Neuroimage*. 2009;44(2):428–47.
47. Bruno JL, Baker JM, Gundran A, et al. Mind over motor mapping: driver response to changing vehicle dynamics. *Hum Brain Mapp*. 2018;39(10):3915–27.
48. Fritz CO, Morris PE, Richler JJ. Effect size estimates: current use, calculations, and interpretation. *J Exp Psychol Gen*. 2012;141(1):2–18.
49. Steffener J, Barulli D, Habeck C, Stern Y. Neuroimaging explanations of age-related differences in task performance. *Front Aging Neurosci*. 2014;6:46.
50. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J R Stat Soc Series B Stat Methodol*. 1995;57(1):289–300.
51. Cohen J. A power primer. *Psychol Bull*. 1992;112(1):155–9.
52. Willcutt EG, Doyle AE, Nigg JT, Faraone SV, Pennington BF. Validity of the executive function theory of attention-deficit/hyperactivity disorder: a meta-analytic review. *Biol Psychiatry*. 2005;57(11):1336–46.
53. Cepeda NJ, Blackwell KA, Munakata Y. Speed isn't everything: complex processing speed measures mask individual differences and developmental changes in executive control. *Dev Sci*. 2013;16(2):269–86.
54. Kibby MY, Vadnais SA, Jagger-Rickels AC. Which components of processing speed are affected in ADHD subtypes? *Child Neuropsychol*. 2019;25(7):964–79.
55. Rassovsky Y, Alfassi T. Attention improves during physical exercise in individuals with ADHD. *Front Psychol*. 2019;9:2747.
56. Caldani S, Razuk M, Septier M, et al. The effect of dual task on attentional performance in children with ADHD. *Front Integr Neurosci*. 2019;2:67.
57. Shorer Z, Becker B, Jacobi-Polishook T, Oddsson L, Melzer I. Postural control among children with and without attention deficit hyperactivity disorder in single and dual conditions. *Eur J Pediatr*. 2012;171(7):1087–94.
58. Manicolo O, Grob A, Hagmann-von Arx P. Gait in children with attention-deficit hyperactivity disorder in a dual-task paradigm. *Front Psychol*. 2017;8:34.
59. Musser ED, Raiker JS. Attention-deficit/hyperactivity disorder: an integrated developmental psychopathology and Research Domain Criteria (RDoC) approach. *Compr Psychiatry*. 2019;90:65–72.
60. Hopfinger JB, Buonocore MH, Mangun GR. The neural mechanisms of top-down attentional control. *Nat Neurosci*. 2000;3(3):284–91.
61. Kim H. Involvement of the dorsal and ventral attention networks in oddball stimulus processing: a meta-analysis. *Hum Brain Mapp*. 2014;35(5):2265–84.
62. Samea F, Soluki S, Nejati V, et al. Brain alterations in children/adolescents with ADHD revisited: a neuroimaging meta-analysis of 96 structural and functional studies. *Neurosci Biobehav Rev*. 2019;100:1–8.
63. Emch M, von Bastian CC, Koch K. Neural correlates of verbal working memory: an fMRI meta-analysis. *Front Hum Neurosci*. 2019;13:180.
64. Al-Saad MSH, Al-Jabri B, Almarzouki AFF. A review of working memory training in the management of attention deficit hyperactivity disorder. *Front Behav Neurosci*. 2021;15:686873.
65. Ogawa A, Kameda T. Dissociable roles of left and right temporoparietal junction in strategic competitive interaction. *Soc Cogn Affect Neurosci*. 2019;14(10):1037–48.
66. Zink CF, Kempf L, Hakimi S, Rainey CA, Stein JL, Meyer-Lindenberg A. Vasopressin modulates social recognition–related activity in the left temporoparietal junction in humans. *Transl Psychiatry*. 2011;1(4):e3.
67. Gallagher HL, Happé F, Brunswick N, Fletcher PC, Frith U, Frith CD. Reading the mind in cartoons and stories: an fMRI study of 'theory of mind' in verbal and nonverbal tasks. *Neuropsychologia*. 2000;38(1):11–21.
68. Ji Z, Feng T, Mei L, Li A, Zhang C. Influence of acute combined physical and cognitive exercise on cognitive function: an NIRS study. *PeerJ*. 2019;7:e7418.
69. Vysniauske R, Verburgh L, Oosterlaan J, Molendijk ML. The effects of physical exercise on functional outcomes in the treatment of ADHD: a meta-analysis. *J Atten Disord*. 2020;24(5):644–54.
70. Szucs D, Ioannidis JPA. Sample size evolution in neuroimaging research: an evaluation of highly-cited studies (1990–2012) and of latest practices (2017–2018) in high-impact journals. *Neuroimage*. 2020;221:117164.