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ORIGINAL ARTICLE

Exercise impact on sustained attention of ADHD children, methylphenidate effects

José A. Medina · Turibio L. B. Netto · Mauro Muszkat · Afonso C. Medina · Denise Botter · Rogério Orbetelli · Luzia F. C. Scaramuzza · Elaine G. Sinnes · Márcio Vilela · Mônica C. Miranda

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Abstract Attention deficit hyperactivity disorder (ADHD) is related to a deficiency of central catecholamines (CA) in cognitive, biochemical, and physical tests, and pharmaceutical intervention may have no effect if it is not accompanied by changes in the environment. The objective of our study was to test the hypothesis that central CA are responsible for the increase in speed reaction seen after physical activity (PA) and to measure the impact of high intensity PA on the sustained attention of 25 children diagnosed with ADHD consistent with the Disease Statistical Mental-IV (DSM-IV) criteria. It is possible that practicing sports assists in the management of the disorder. The children were divided between users (US) and non-users (NUS) of methylphenidate (MTP), and the groups were compared to evaluate the effect of the drug on cognition after PA. Post-exercise performance on Conner's Continuous Performance Test-II (CPT) was not affected by MTP, we observed significant improvements in response time, and we saw normalization in the impulsivity and vigilance measures. These results suggest that the improvements in cognition after physical effort are not CA dependent. Additionally, our results suggest that children's attention deficits can be minimized through PA irrespective of treatment with MTP. Additional studies are necessary to confirm that exercise mitigates the harmful symptoms of ADHD.

Keywords Exercise · CPT · ADHD · Sports · Sustained attention · Physical activity

J. A. Medina (✉) · T. L. B. Netto · R. Orbetelli
Medicine Centre of Physical Activity and Sport (CEMAFE), Federal University of São Paulo, São Paulo, SP 4005-040, Brazil
e-mail: j.a.medina@terra.com.br

T. L. B. Netto
e-mail: barrosturibio.cemafe@epm.br

R. Orbetelli
e-mail: rogerio@cemafe.com.br

M. Muszkat · L. F. C. Scaramuzza · E. G. Sinnes · M. C. Miranda
Child's Neuropsychological Attendance Center (NANI), Federal University of São Paulo, São Paulo, SP, Brazil
e-mail: nani@psicobio.epm.br; mauromuszkat@uol.com.br

L. F. C. Scaramuzza
e-mail: flaviacoelho2000@hotmail.com.br

E. G. Sinnes
e-mail: elainegsinne@gmail.com

A. C. Medina
Department of Cardiology, Engineer School, University of São Paulo, São Paulo, SP 4023-004, Brazil
e-mail: cardio.dmed@epm.br; afmedina@uol.com.br

D. Botter
Department of Cardiology, Intitute of Math, University of São Paulo, São Paulo, SP 4023-004, Brazil
e-mail: botter@ime.usp.br

M. Vilela
Department of Cardiology, Physical School, Federal University of São Paulo, São Paulo, SP 4023-004, Brazil
e-mail: marciomvilela@hotmail.com.br

Introduction

Attention deficit hyperactivity disorder (ADHD) is the most prevalent childhood psychiatric disorder (Nair et al. 2006). The symptoms, usually associated with a variety of psychiatric comorbidities (Souza et al. 2001), are related to a catecholaminergic dysfunction in the prefrontal cortex and striatal areas, as shown by image and neurobiological studies (Hendren et al. 2000). Children with ADHD also peripherally exhibit catecholamine (CA) deficiencies, which can be detected during biochemical (Girardi et al. 1995), physical (Wigal et al. 2003), and cognitive tests (Anderson et al. 2000).

Methylphenidate (MTP) is the drug most often used for the treatment of ADHD. It is a CA stimulant with the duration of action from 1 to 4 h and a short half-life (2–3 h; Quay 1997), which improves behavior in 80–85% of the ADHD population (Kimko et al. 1999).

Clinical response to MTP is associated with improved interaction of CA and respective receptors on cortex prefrontal and striatal areas (Berridge et al. 2006). Many authors attribute the same mechanism for improvements on the speed of reaction seen immediately after PA practice on asymptomatic individuals (McMorris et al. 2008). Notwithstanding the failure of proving these neurobiological findings after PA on humans (Nybo et al. 2003; Wang et al. 2000), the elevation of CA on striatal areas of brain is well established in animal models (Hattori et al. 1996; Meeusen et al. 1997; MacRae et al. 1987; Freed and Yamamoto 1985; Hattori et al. 1994).

Besides the CA hypothesis of an acute exercise–cognition interaction, other evidence that support PA on management of ADHD children is the number of research showing that PA practice is associated with lower levels of psychiatric disorders, which are commonly related to ADHD comorbidities.

The beneficial effects of PA on mental function and wellness are seen in school-age children as well as adults. In children, physical exercise presents negative correlations with anxiety, disorders of mood and behavior, and academic underperformance (Strong et al. 2005).

Studies of acute physical effort in asymptomatic individuals have demonstrated a positive correlation between various types of acute PA, with different loads, duration times, and cognitive tasks (Tomporowski 2003; Brisswalter et al. 2002).

Majority of articles about PA and brain show the beneficial effects of an active lifestyle on mental health, cognition, and emotion (Koehl et al. 2008).

Neuroplasticity also has been associated with PA. Several brain structures, like the hippocampus (Cotman and Berchtold 2002), a key structure for higher cognitive function and stress-related pathologies (Kim and Diamond 2002), have been connected with and mediated by peripheral levels of brain-derived neurotrophic factor (BDNF), thus improving short-term learning success after intense exercise.

BDNF is a protein that acts on definite neurons of the central nervous system and the peripheral nervous system, supporting the survival of existing neurons and promoting the growth and differentiation of new neurons and synapses (Acheson et al. 1995). In the brain, it is active in the hippocampus, cortex, and basal forebrain—areas vital to learning, memory, and thinking (Yamada and Nabeshima 2003). BDNF itself is important for long-term memory (Bekinschtein et al. 2008).

BDNF-dependent neurogenesis induced by exercise requires the release of beta-endorphins, which is normally associated with intense physical activity (Schwarz and Kindermann 1990) and is a contributing factor in mental health associated with exercise (Koehl et al. 2008).

While importance of the BDNF on cognitive aspects after PA is recognized, peripheral levels of dopamine and epinephrine after PA were found to have stronger correlations with intermediate and long-term learning, respectively, than with BDNF (Winter et al. 2007), suggesting the main role of CA on cognitive aspects seen after exercises.

Regardless of the underlying mechanisms responsible for this observation, it motivates a discussion on whether findings of better cognitive and brain health in more active persons are caused by PA or whether healthy individuals are more likely to lead an active life.

The potential benefits of PA in children with ADHD are far from clear, and the few studies that have attempted to gain insights to date lack precise diagnoses and appropriate psychological testing (Tantillo et al. 2002).

The aims of the present study are to examine the possibility that PA may improve sustained attention among ADHD children and to test the CA hypothesis of an acute exercise–cognition interaction (McMorris et al. 2008). Based on data that children with ADHD have a cathecolaminergic dysfunction and that the cognitive gains observed during and after practice are dependent on the integrity of this neurobiological system, it is expected that children with ADHD will not show the same cognitive results usually seen in asymptomatic individuals with better reaction times in cognitive tasks (Tomporowski 2003; Brisswalter et al. 2002). It is particularly important to describe cognitive effects in ADHD children after exercise because of the high prevalence of the disorder. In addition, treatment with MTP, although it is well established, offers no long-term benefits (Jensen et al. 2007; Weiss et al. 1975).

Methods

This study was approved by the Ethics Committee of the Federal University of São Paulo (UNIFESP). Approval was obtained from the parents or guardians of all research participants. All of the children who participated in this research, 25 boys, had been diagnosed with ADHD and had received prescriptions for MTP; however, nine of these participants chose not to use MTP because of financial concerns, a fear of adverse events, or difficulty obtaining the drug. Thus, we analyzed physiological responses to an ergospirometric test and cognitive responses after physical effort in 16 users (US) and nine non-users (NUS) of MTP. We choose school-age males because the psychiatric disorder is more frequent in boys and the diagnosis often is made in this age.

A between-group, US and NUS, comparison of the children's attention immediately after physical effort was designed to help us better understand the chronic effects of psychostimulants and whether they cause any change in Conner's Continuous Performance Test-II (CPT) immediately after exercise. A Vacuumed TurboFit V4.047 gas analyzer, treadmill, and Precor 964i Filizola scales were calibrated before each assessment. Ergospirometry was performed by fitting the participants with masks.

Subjects

All research participants were informed of the study risks by their families and by representatives of the Department of Neuropsychological Child Services (NANI). We enrolled 25 male participants aged 7–15, the mean and the standard deviant of US and NUS were 9.33 and 2.87, 9.75 and 2.38, respectively. Fifteen patients received MTP in doses of 5 or 10 mg per day, depending on their therapeutic response. The average dose was 0.27 mg/kg. One boy received 30 mg per day. Of the nine children to whom the drug was not administered, one had been exposed to the drug for over 1 year before being enrolled in our study.

Some participants had been receiving other psychoactive substances, such as carbamazepine, valproic acid, and lamotrigin. The most common types of recreational activity engaged in by the subjects were soccer and cycling. Children were not excluded from the study based on psychiatric comorbidity, sporadic attacks of asthma, or allergic rhinitis. The stage of pubic hair development was based on the criteria of Tanner (1962) and was assessed by a pediatrician experienced in the assessment of secondary sex characteristics. In the group of US, 11 were classified as pubic hair Stage 1, two boys classified as Stage 2, one boy as Stage 3, and two boys as Stage 4. Among the NUS, seven boys were classified as Stage 1, one boy as Stage 3, and one boy as Stage 4.

Based on skin color, the majority of the subjects had mixed characteristics of two or more ethnicities. The participants were classified as 19 predominantly Caucasians, three predominantly negroid, and three with mixed Caucasian and negroid phenotypes.

Diagnosis of ADHD

The diagnosis was made using the Diagnostic and Statistical Manual of Mental Disorders-fourth edition, DSM-IV, criteria and a battery of neuropsychological tests, including the Digit Span test in direct and reverse order, Rey figure drawing, Child Behavior Checklist completed by each child's parents, the EACI Scale-P completed by teachers who had worked with the children, the WECHSLER Intelligence Scale for Children, and Conner's Continuous Performance Test-II (CPT). Oppositional, cooperative, and dysfunctional behaviors were observed in individuals and groups of 3–4 children through storytelling and exercises in collaborative design. Additional criteria for the diagnosis of ADHD included the presence of symptoms in two or more settings before the age of seven. Diagnoses were confirmed by a neuropediatrician after multidisciplinary evaluations by a neuropsychologist, child psychiatrist, and psychopedagogists.

Participants eligible for inclusion were males who had been diagnosed with ADHD with a confidence interval $\geq$50 (this metric represents the likelihood of a child actually having ADHD according to their clinical profile on the CPT task), had been prescribed MTP, and exhibited no clinical comorbidities that could compromise the experiment. A 48 h period was allowed between MTP administrations and testing.

Experimental setup

Each child completed two visits to the Medical Center of Physical Activity and Sport (CEMAFE), which is connected to the UNIFESP. During the first visit, each child was weighed, measured, and subjected to an ergospirometric test on a treadmill with increasing speed and slope until exhaustion. Oxygen consumption was measured under constant electrocardiographic monitoring every 30 s to determine the peak of consume of oxygen (VO_2). We determined the ventilatory threshold 1 (LV_1) by monitoring the overshot of minute ventilation (VE) in relation to the increase in VO_2, the lower percentage point of oxygen, and the high rise in VE (Reybrouck et al. 1985). We recorded the heart rate (HR) in bpm at LV_1 and the maximum HR (max), and we determined the HR target by subtracting HR LV_1 from HR max, multiplying by 0.25, and adding the HR LV_1.

Approximately 1 month later, each child was subjected to an exercise protocol already applied in children with cystic fibrosis and children with ADHD (Wigal et al. 2003). It included 10 loads of effort for 2 min interspersed with 1 min of rest, for a total of 30 min of activity. The protocol was carried out on a treadmill because our facility was unable to provide access to a cycle ergometer. The physical tests were carried out in the presence of physical education instructors, sports doctors, and nurses. Speed and inclination were modified for each child in order to reach his target HR. A maximum of 1 h before the test, a 6% isotonic solution was administered to all subjects. Immediately after the test, each patient was directed to an isolated room where neuropsychologists administered the CPT. All of the patients who were receiving MTP had the drug withheld for 48 h.

The CPT assesses sustained attention and helps with both diagnosis and clinical follow-up. Its outcome can be altered when a patient is receiving MTP, mainly due to the Commissions and Omissions, two cognitive variables present in the CPT (Losier et al. 1996). The CPT was applied three times: at diagnosis, after exercise, and after a 1 min stretching session (SS) used as a control measure. The neuropsychologist administered the test after briefly explaining the procedure. The CPT was applied by NANI diagnostically and after the stretching session (quadriceps and triceps bilaterally, 15 s per muscle). The CPT post-effort tests were administered at CEMAFE by neuropsychologists. None of the patients were receiving MTP during the diagnosis stage, and all of the patients who were receiving MTP had the drug withheld for 48 h before all tests, both cognitive and physical.

Conner's continuous performance test-II

The CPT-II is highly sensitive to ADHD children, represents an advance in relation to others types of CPTs, and allows the collected information, including 13 different variables, to be compared with a database ADHD group and with a control group without ADHD symptoms. CPT is a computerized assessment characterized by the rapid presentation of a continuously changing stimulus (non-X letter), which the child may click, among which there appears a designated "target" (X-letter), which the child may not click, the duration of task is about 14 min. We describe below each measure of the CPT.

Omissions represent the number of times that the assessed individual should have clicked a non-"x" letter, but did not do so. Commissions represent the number of times when the assessed individual should not have clicked the letter "x", but did so. Hit reaction time (RT) was defined as the mean overall reaction time for correct clicks. Both high and low Hit RT scores can be significant; low scores (unusually fast RTs) may be associated with impulsivity, and high scores (unusually slow RTs) may indicate inattentiveness.

The Hit standard error (SE) RT is a measure of response speed consistency. The higher the Overall Standard Error, the greater the inconsistency in the response speed. Variability of Standard Error like Overall Standard Error, the Variability of Standard Error is a measure of response speed consistency. However, variability of Standard Error measures "within respondent" variability. That is, the amount of variability the individual shows in 18 separate segments of the test in relation to his or her own overall standard error. Detectability (d') measures the capacity to discriminate "x" from non-"x" and is calculated by the difference between the click distributions (omission) and false alarms (commission) already described (Losier et al. 1996). Style indicator B captures the natural propensity of some individuals who are reluctant to click the letter "x" to delay their responses, avoiding the reduction in precision that would be observed if the individual answered as quickly as possible. High values indicate that the assessed individual did not engage in this behavior, while low values indicate that the participant delayed his responses. High and low B scores are both noteworthy and indicate unusual response styles.

Perseveration is a measure of CPT decrypted like any reaction time less than 100 ms. Given normal expectations of physiological ability to respond, such responses are usually either slow responses to a preceding stimuli, a random response, an anticipatory response, or a response repeated without consideration of the stimuli or task requirements.

Hit RT Block Change assesses changes in reaction time as the test progresses. The Hit SE Block Change assesses the consistency of the previous measurement.

The Hit RT Interstimulus (ISI), this measure examines change in average reaction times at the different Inter-Stimulus Intervals (when the letters are presented in 1, 2, or 4 s).

Hit SE ISI Change examines the consistency of the reaction time as a function of the time of the appearance of the letters. Commissions, Hit RT, and Perseveration are impulsivity measures. Hit RT Block Change and Hit SE Block Change are vigilance measures.

Effects of MTP on ergospirometry and CPT post exercise

Table 1 shows physiological, anthropometric, and confidences indices of US and NUS. The confidence indices is a variable of CPT that allow clinical monitoring and predict the probability of a patient presenting with ADHD, taking into account the US and NUS metrics, as well as the associated *P*-values. We described them to show that the similarity between US and NUS is not only in anthropometric but also in attentional data. Table 2 lists the cognitive values recorded in the US and NUS groups after the exercise protocol and the *P*-values.

Table 3 shows data from the 25 post-exercise attentional tests compared with the post-SS results and their significance.

Data analysis

This research is basically the result of two statistical analyses. The first analysis is the comparison, between 16

Table 1 Anthropometric, ergoespirometric, and CPT values in NUS and US, and statistical significance

	NUS $n = 9$			US $n = 16$			(P)
	Media	95% CI	SD	Media	95% CI	SD	
Age (years)	9.33	12.16, 6.23	2.87	9.75	11.02, 8.48	2.38	0.35
Weight (Kg)	38.43	60.96, 19.75	15.91	38.18	33.77, 20.03	17.69	0.67
Height (cm)	139.83	163.52, 112.87	21.20	140.61	142.83, 117.13	15.40	0.36
BMI kg/m^2	19.04	23.80, 17.40	2.79	18.58	18.32, 13.46	4.94	0.51
VO_2 peak	43.80	53.00, 31.27	7.75	43.36	51.67, 31.96	5.21	0.85
LV1/VO_2	32.01	44.52, 24.46	7.63	29.30	43.35, 19.24	7.81	0.20
LV1/FC	160.56	181.60, 149.19	20.30	158.06	176.41, 146.78	14.15	0.37
LV1/%VO_2	74.21	100.96, 63.26	17.12	67.32	92.69, 55.01	15.98	0.17
HR peak	195.00	199.87, 185.33	7.62	186.68	203.74, 174.26	15.08	0.04*
BPS peak	141.43	156.42, 119.58	24.34	122.86	150.42, 113.58	24.31	0.05
MCOx peak	27,390.00	31,096.67, 23,683.32	4,007.88	23,512.14	26,540.58, 20,483.72	5,245.11	0.05
BPD peak	42.86	81.20, −21.20	24.36	45.00	86.46, −6.46	24.38	0.71
BPM peak	64.29	97.33, 31.23	24.40	70.95	93.11, 57.36	24.42	0.34
HR target	169.00	178.09, 165.11	14.91	165.31	182.05, 155.15	13.63	0.27
PA (min)	25.00	30.22, 20.77	5.50	26.31	29.61, 21.14	5.21	0.28
Energy expe	363.97	524.90, 262.89	131.74	322.76	422.59, 230.33	89.12	0.21
Índex.confid/diag	83.18	95.39, 70.96	15.89	77.68	83.72, 58.47	15.92	0.20
Índex.confid/PA	62.63	72.28, 52.98	12.56	60.18	55.79, 45.42	12.60	0.33
Índex.confid/SS	63.35	76.29, 50.39	16.84	73.67	75.21, 51.38	16.87	0.08

Anthropometric, ergospirometry, pressure, and cognitive data are presented in terms of their means, confidence interval (CI), and standard deviations (SD). VO_2 is in ml/kg/min, LV_1/VO_2 represent the consumption of O_2 in ml/kg/min to LV_1, LV_1/HR to HR in LV_1, $LV_1\%/VO_2$. BPS is the systolic blood pressure measured in the first minute after ergospirometry in mmHg, BPD is the diastolic blood pressure in mmHg, and MAP denotes mean arterial pressure (measured under the same conditions as the BPS). The energy expenditure is expressed in Kcal expended in 1 h at the estimated effort intensity of LV_1. MCOx is miocardic consume of oxygen, product of BPS after maximal effort and HR peak*. Index.confid is confidence index. (P) is P-value

Table 2 CPT-II differences between US and NUS after physical load

	US			NUS			(P)
	Mean	95% CI	SD	Mean	95% CI	SD	
Omissions	22.68	40.20, 10.23	16.72	21.55	30.93, 12.17	12.19	0.42
Commissions	25.18	30.96, 19.03	7.13	24.44	30.94, 17.94	8.45	0.81
Hit RT	417.83	462.10, 366.97	56.49	436.51	487.85, 385.17	66.78	0.24
Hit RT std. error	14.68	20.47, 9.59	6.32	16.21	22.08, 10.35	7.63	0.30
Variability	34.52	56.85, 15.10	22.90	35.48	51.36, 19.59	20.66	0.45
Detectability (d')	0.26	0.56, −0.11	0.35	0.41	0.71, 0.12	0.38	0.16
Response style (B)	1.19	2.78, 0.36	1.24	0.65	0.89, 0.42	0.30	0.08
Perseverations	14.25	31.84, 2.37	16.50	14	21.57, 6.42	9.84	0.48
Hit RT block change	0.02	0.05, 0.009	0.03	0.03	0.05, 0.008	0.03	0.35
Hit SE block change	0.05	0.13, 0.0001	0.10	0.08	0.16, −0.005	0.11	0.27
Hit RT ISI change	0.07	0.13, 0.03	0.05	0.10	0.15, 0.05	0.06	0.15
Hit SE ISI change	0.16	0.35, 0.005	0.21	0.14	0.32, −0.02	0.23	0.43
Índex confid	60.17	55.79, 45.42	15.34	62.63	72.28, 52.98	12.55	0.34

The CPT variables are described by their means, interval confidence, and standard deviations. No significant differences were apparent between any measures. However, the B-style response differences approached significance

Table 3 Comparison between PA and SS on CPT-II responses, $n = 25$

CPT-II	Physical activity			Control			(P)
	Mean	95% CI	SD	Mean	95% CI	SD	
Omissions	22.28	28.46, 16.09	14.98	27.44	39.26, 15.61	28.64	0.14
Commissions	24.92	28.00, 21.83	7.47	24.6	27.81, 21.38	7.77	0.23
Hit RT	424.55	449.20, 399.90	59.71	451.38	486.05, 416.70	84.00	0.01*
Hit RT std. error	15.23	18.00, 12.46	6.7	19.17	23.27, 15.06	9.3	0.01†
Variability	34.86	43.82, 25.91	21.68	44.45	55.26, 33.63	26.20	0.05
Detectability (d')	0.31	0.47, 0.16	0.36	0.24	0.38, 0.10	0.33	0.08
Response style (B)	0.99	1.42, 0.57	1.03	0.96	1.16, 0.77	0.47	0.33
Perseverations	14.16	20.03, 8.28	14.23	34.48	51.15, 17.80	40.40	0.004‡
Hit RT block change	0.03	0.04, 0.01	0.03	0.02	0.05, 0.002	0.05	0.38
Hit SE block change	0.06	0.10, 0.02	0.1	0.07	0.13, 0.01	0.14	0.36
Hit RT ISI change	0.08	0.11, 0.06	0.05	0.11	0.14, 0.09	0.06	0.006§
Hit SE ISI change	0.15	0.24, 0.06	0.21	0.20	0.27, 0.13	0.17	0.10
Index confid	61.06	66.91, 55.20	14.18	69.95	77.31, 62.58	17.84	0.007‖

The results show statistical improvements in the index of confidence ‖ and vigilance measures of post-exercise *hit reaction time, †hit reaction time standard error, §hit reaction time interstimulus and the impulsivity measure of ‡perseveration compared with SS in the subsequent month

US and 9NUS, of anthropometric, physiological and cognitive data (CPTs at the moment diagnostic, after PA and after SS, respectively). The second analysis is the comparison of cognitive variables seen on CPT after a SS and PA, with all participants together.

All data, physiological and cognitives were tested with respect to the normality. The concomitant finding of non-normal distribution with Kolmogorov–Smirnov and Shapiro–Wilk tests lead us to use a non-parametric test, Wilcoxon Signed Ranks Test to determine the significance of our results. The variables with normal distribution were tested before with F-test, to identify similarity or different variances, and then an adequate t-test was applied: t-tests with presumed similar, different variances, or paired t-test. All data were analyzed using Microsoft Excel 2003 and PASW statistics 18, $P < 0.05$ was chosen as the significance criterion.

We compared the CPT measures obtained after exercise for both the US and NUS groups. In the absence of significant differences between data from children who were and were not receiving MTP, the post-exercise and post-SS CPT data were compared for the combined cohort of 25 subjects. Simple linear regression was used to test the strength of the associations between the physiological and cognitive parameters.

Results

All physiological variables had normal distribution except: weight, index body mass, diastolic blood pressure, and maximal consumption of oxygen. The variables of CPT had normal distribution except commission and style B. To these cognitives and physiological cases, a non-parametric test was applied Wilcoxon Signed Ranks Test. All data with normal distribution showed to F-test similar variances, except heart hit máx.

Characteristics of study participants

Table 1 shows that children with ADHD, in both the US and NUS groups, had anthropometric, weight, and height data compatible with the 75th percentiles of curves derived from national standards (Marcondes et al. 1969) and 50th percentiles of international standards (Tanner and Davies 1985). The ergospirometry and cognitive data were largely homogeneous. There were significant differences in maximum HR between the two groups immediately after the ergospirometric test. The myocardial oxygen consumption and systolic blood pressure (SBP) comparisons had two fewer participants, with a final sample of 14 participants in the US group and nine in the NUS group. The cognitive parameters did not differ statistically.

CPT post-exercise comparisons between US and NUS

Table 2 shows that there were no differences between the two groups, but the typical US response was more conservative, with an emphasis on not making mistakes, compared with the NUS strategy, which was to accumulate more clicks, as shown by the Style B notation. All 25 participants exhibited similar CPT results, irrespective of the chronic effects of MTP treatment.

CPT-II post-exercise and SS, US, and NUS

The means and standard deviations of the 12 variables are shown in Table 3. The respective *P*-values are shown where relevant.

Cognitive-relations exercise stress test

The regression analysis showed that neither the VO_2 nor the LV_1, nor their inter-relationships, are related to better cognitive performance.

Stretching as control

The values obtained after stretching were compared with those collected after exercise. This was deemed necessary because the measures taken at diagnosis may have been inappropriate, owing to differential motivational circumstances between participants. We decided that a brief stretching session would be representative of the natural buoyancy of attention and executive function.

Discussion

This study examined the effect of MTP on the cognitive responses seen immediately after the exertion of physical effort and the physiological differences observed during and after a maximum run on a treadmill between the US and NUS groups, containing 16 and 9 boys, respectively. We also described the impact on the sustained attention of 25 children with ADHD of the use of CPT and a protocol of suprathreshold bouts of exercise for longer than 20 min, currently accepted in children with physiological difficulties like fibroses cystic (Wigal et al. 2003).

We concluded that the chronic use of MTP was associated with significant physiological and attentional effects despite our small sample size and the short period of administration of the drug. We identified lower values of max HR in those treated with drugs ($P = 0.04$), and we reached almost the same conclusion for SBP ($P = 0.05$) immediately after exercise. The vast majority of articles addressing physiological responses to exercise and MTP have noted the opposite effect on HR (Mahon et al. 2008; Werry and Aman 1975; Baillard et al. 1976; Boileau et al. 1976) with acute MTP therapy taken before performing the physical effort. The inherent brain mechanisms and the cardiovascular effects of MTP are not clear. MTP blocks the DA and norepinephrine transporters (Kuczenski and Segal 1997), and the prevailing view is that its cardiovascular effects are mediated primarily through norepinephrine stimulation, but some research suggests otherwise. The cardiovascular effects of cocaine, a drug pharmacologically analogous to MTP that also blocks DA and norepinephrine transporters, are mediated in part by DA (Tella and Goldberg 1998). DA contributes to cardiovascular regulation via central and peripheral mechanisms (van den Buuse 1998), the stimulation of cells in the ventral tegmental area, a dopaminergic area, and incremental BP, and these effects are antagonized by the DA D2 receptor blocker raclopride, raising the possibility that DA regulates this function is in part mediated via peripheral catecholamines (Mannelli et al. 1997).

It is likely that our results are caused by the acute adaptive phenomenon of tolerance, which is commonly related to the effects of dopaminergic medications such as MTP (Swanson et al. 1999). The immediate use of a psychostimulant elevates the HR and BP, but in chronic users, when it is not used before maximal exercise, the opposite effect was observed. This could reflect peripheral adaptation responses that counteract the central effects on cardiovascular function. Nevertheless, the physiological associations between central CA, the brain, HR, and BP have not all been elucidated. Some researchers have shown that cardiovascular effects of MTP in humans are associated with central increases in DA and epinephrine in plasma (Volkow et al. 2003), similar to the effects of PA. These results are consistent with the hypothesis that DA may also be involved in maintaining cardiovascular homeostasis in humans during PA.

Moreover, when the two measured variables, SBP and HR, which almost reached significance at maximal effort, are multiplied, they provide an indirect measure of myocardial oxygen consumption (Miranda et al. 2005) that was also not significantly reduced by weekly administration of MTP ($P = 0.05$).

MTP did not appear to have any different influences on the CPT cognitive effects after PA when a comparison was made between the US and NUS groups, except for the style of response ($P = 0.05$). Participants in the US group exhibited a conservative strategy evoked by their drug treatment, which causes anxiety, and because of the motivation to improve their performance on the neuropsychological tests for the sake of their family and clinical staff.

An analysis of attention after exercise and stretching showed that among 25 boys with ADHD, ignoring MTP use, exercise resulted in (a) increased surveillance, (b) decreased impulsivity, (c) increased reaction speed, and (d) greater stability in all of the aforementioned metrics.

These preliminary results differ from previous results obtained by Klein and Deffenbacher (1977). They found no cognitive differences in hyperactive children when modeling clay, as a control measure, or when these children were submitted to physical effort or relaxation, as diagnosed by Conner's scale (1969) criteria. The researchers used a shortened version of the CPT to observe the cognitive variation after PA. Perhaps the 10-min duration of the physical power and agility test and the intensity of effort, which was not controlled by these researchers, could explain the results obtained. The significant improvements argued for by this author after both relaxation and PA occurred when he compared these two management techniques with a no-treatment control.

Craft (1983) compared the cognitive results of 31 hyperactive and 31 asymptomatic controls after pedaling a bicycle ergometer for 0, 1, 5, and 10 min. The participants were diagnosed by Conner's Abbreviated Teacher Rating Scale. The cognitive impact of PA was assessed by three neuropsychological tests that verify executive functions, the Digit Span, Coding B of the Wechsler Intelligence Scale for Children, Revised version, and the Illinois Test of Psycholinguistic Abilities-Visual Sequential Memory. The intensity of the exercise was monitored so that heart rate remained steady at about 170 bpm. None of the test measures showed any statistical improvement after PA when compared with adequate controls. We believe that the types and durations of the neuropsychological tests were responsible for the failure of the results. The participants did not use medications in either of the studies. Tantillo et al. (2002) tried to show dopaminergic effects through spontaneous eye blinks and the acoustic startle eye blink response after PA in ADHD children and asymptomatic controls. They found increased spontaneous eye blinking and decreased acoustic startle eye blinking latency in ADHD boys after vigorous exercise. The two measures are positively correlated with DA levels in the caudate nucleus and striatum, respectively; however, the statistical inferences do not allow a definitive conclusion that exercise has a dopaminergic effect.

Our results in no way differ from those observed among normal individuals immediately after exercise; that is, better reaction times (Tomporowski 2003). Our findings refute the theory that central CA is the factor responsible for PA-induced improvements in reaction time. Moreover, detectability, a variable of the CPT that can be improved by acute MTP administration with more sensitivity than omissions and commissions in isolation (that is, it is calculated via an equation in which these two variables are the only independent variables; Hochhaus 1972), showed improvement at a level approaching significance ($P = 0.08$).

Another PA-induced improvement, impulsivity, was lower after exercise; however, this improvement, evidenced by perseveration, has low retest reproducibility (0.59; Conners and Staff 2000).

These results suggest that sports similar to the activity employed in our protocol, that is, glycolytic and aerobic exercises, may improve the sustained attention of these children. The cognitive effects induced by PA may be much more important than the explicit measures of glycogen storage, oxygen consumption, or lactate values and may ameliorate the differences between ADHD children and their colleagues, as well as improve their self-esteem. Some popular sports like judo and soccer, with periodical anaerobic loads and an aerobic basis, similar to our protocol, could help these children to diminish their symptoms and may teach them to respect rules, to win and to lose, to improve their reaction time, and other skills that these sports require, aiding prefrontal development. However, our results do not support the conclusion that learning is maximized or that PA can replace MTP therapy. Nevertheless, we would suggest that exercise may be an easy way to make treatment more accessible.

The questions raised in the introduction of this article seem to have been answered. PA can improve the sustained attention of ADHD children, and in view of the similarity between the cognitive responses seen after PA in ADHD and asymptomatic children, the cathecolaminergic theory explaining improvements in reaction time after exercise appears not to be reasonable.

Nevertheless, when our results are added to the existing scientific and anthropological literature, an old paradigm arises. Chen et al. (1999) found that DRD4/7R alleles, related to the transcription of DRD4, a dopamine receptor related to many symptoms of ADHD (Li et al. 2006), are more frequent in nomadic people than in settled populations. There is evidence that the minor alleles of DRD2 and DRD4 (A1 and 7R, respectively) decrease the sensitivity and/or concentrations of their respective receptors (van Craenenbroeck et al. 2005). Hence, minor alleles are analogous to their respective DA receptor antagonists. DRD2 and DRD4 are both considered D2-like receptors and have similar functions and distributions. DRD2 seems to be important in the striatum, and DRD4 appears to be important in the prefrontal cortex.

The two alleles are involved in the characteristic ADHD symptoms of impulsivity, reward anticipation, and addiction. The alleles may interact in a complex manner to express their effects (Eisenberg et al. 2007). When a comparison of these genes is made between settled-sedentary and nomadic people, the latter show better nutritional indices than the former. This nutritional advantage is related to free fat mass (Eisenberg et al. 2008), represented mainly by muscles, which results from adequate physiological adaptation to a specific load, usually physical activities, with sufficient rest and food.

ADHD children show lower lactate values than asymptomatic controls under similar intensities of PA (Wigal et al. 2003), and therefore, ADHD persons may, theoretically, be at an advantage in aerobic sports, considering that the concentration of lactic acid, which is expressed in ventilation by the lactate threshold

(Wasserman and McLlory 1964), is inversely related to endurance performance (Farrel et al. 1979; Tanaka and Seals 2008). Moreover, the DRD4\7R allele was associated with more extensive migration over the past 1,000 and 30,000 years (Chen et al. 1999) and was positively selected for between 40,000 and 50,000 years ago (Wang et al. 2000, 2004); therefore, it seems rational that the active lifestyle, added to the already discussed advantages to health, likely result from a period of time during which the phenotype of these individuals was adaptive.

Finally, our research speaks to a philosophical question; the dividing line between madness and reason becomes a question of whether ADHD is an advantage or a disease depending on the environment in which the affected person lives.

ADHD is a clinical condition with various associated psychiatric comorbidities (Goldman et al. 1998) and a severe social impact (Rösler et al. 2004). Pharmacological treatment is well recognized to attenuate symptoms and to have neurobiological specificity (Spencer et al. 2000), but there is still no cure for the condition.

This study has some restrictions: effect of PA has not been examined on other aspects of attentional dysfunction of children with ADHD; no analysis of ADHD subgroups was made because of small sample sizes and this research had no control of effects by a healthy control group.

Conclusion

In summary, we found that the CPT response to exercise was improved in children with ADHD (children with attentional problems detected by CPT and that received MTP prescription), after acute bouts of PA suprathreshold arise 20 min, when compared to a SS, our control measure.

Our data suggest that the cognitive improvements seen after exercise are probably not caused by central CA elevation. However, PA is a promising way to achieve improvement in the symptoms of ADHD. Additional studies are necessary to confirm that exercise mitigates the harmful symptoms of ADHD.

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