

2017

# Effects of Two-Week High-Intensity Interval Training on Cognition in Adolescents - A Randomized Controlled Pilot Study

Stenman Mari

Walter de Gruyter GmbH

---

<info:eu-repo/semantics/article>

<info:eu-repo/semantics/publishedVersion>

© Human Movement

CC BY-NC-ND <https://creativecommons.org/licenses/by-nc-nd/4.0/>

<http://dx.doi.org/10.1515/humo-2017-0019>

---

<https://erepo.uef.fi/handle/123456789/5042>

*Downloaded from University of Eastern Finland's eRepository*



# EFFECTS OF TWO-WEEK HIGH-INTENSITY INTERVAL TRAINING ON COGNITION IN ADOLESCENTS – A RANDOMIZED CONTROLLED PILOT STUDY

original paper

doi: 10.1515/humo-2017-0019

MARI STENMAN<sup>1</sup>, ARTO J. PESOLA<sup>1</sup>, ARTO LAUKKANEN<sup>1</sup>, EERO A. HAAPALA<sup>1,2</sup>

<sup>1</sup> Faculty of Sport and Health Sciences, University of Jyväskylä, Jyväskylä, Finland

<sup>2</sup> Faculty of Health Sciences, University of Eastern Finland, Kuopio Campus, Finland

## ABSTRACT

**Purpose.** We investigated the effects of a two-week high-intensity interval training (HIT) on cognition in adolescents.

**Methods.** The participants were recruited from local high schools with an electronic messaging system. The HIT group participated in 4 high-intensity interval running sessions and 2 circuit training sessions. The control group (CG) continued their usual habits. Reaction time, choose reaction time, working memory, visual memory, and learning were assessed by computerized CogState test battery. The intervention effect was investigated with repeated measures ANOVA and the effect size by Morris  $d_{ppc2}$ .

**Results.** The total of 25 participants aged 17–20 years participated in the baseline measurements and were randomized into the intervention ( $n = 12$ ) and control ( $n = 13$ ) groups; 9 people in the HIT group and 10 in the CG also participated in the follow-up assessments. Reaction time (mean change [SD] = 0.02 [0.03] vs. -0.05 [0.08],  $p$  for time\*group interaction = 0.025,  $d_{ppc2} = -0.297$ ) and choice reaction time (0.03 [0.03] vs. -0.01 [0.04],  $p$  for time\*group interaction = 0.017,  $d_{ppc2} = -0.874$ ) improved more in the CG than in the HIT group. While we found no other statistically significant time\*group interactions, intervention turned out to have a small negative effect on working memory ( $d_{ppc2} = -0.470$ ) and a small positive effect on visual memory and learning ( $d_{ppc2} = 0.419$ ).

**Conclusions.** The study on HIT produced mixed effects on cognition in adolescents. Studies with a longer intervention period and larger sample sizes are warranted to further explore HIT effects on cognition.

**Key words:** youth, physical activity, exercise, fitness, cognition

## Introduction

Physical inactivity causes an enormous public health and economic burden in developed countries [1]. Approximately half of the children meet the recommended levels of physical activity (PA) and the number of sufficiently active adolescents decreases with increasing age [2]. Inadequate levels of PA have been related to an increased risk of cardiovascular diseases and type 2 diabetes already in childhood [3]. They are also associated with poorer cognition and academic achievement in children and adolescents [4]. Interventions aiming to increase PA levels and thereby decrease inactivity-related cardiometabolic risk factors in children and adolescents have been relatively ineffective [5]. Thus high-intensity interval training (HIT) has been suggested as an alternative mode of PA to improve health in children and adolescents [6, 7]. However, the evidence on the effects of HIT on cognition in adolescents is limited.

A single HIT session is typically shorter than 30 min-

utes and consists of short high-intensity work periods lasting from a few seconds to several minutes, separated by relatively short active or passive recovery periods [8, 9]. Exercise intensity in HIT may be maximal, but recent studies have suggested that nearly maximal (85–95% of maximal heart rate) HIT has similar health and fitness benefits as maximal HIT [8].

Higher levels of PA have been associated with better cognition in children and adolescents [4]. The results of one study also suggested that vigorous intensity PA may have a stronger relationship with cognition than light-to-moderate intensity PA in adolescents [10]. Therefore, HIT may provide an effective stimulus to improve cognitive functions among youth. However, the evidence from intervention studies on the effects of PA on cognition in adolescents is limited [11] and a few studies have investigated the impact of HIT on cognition in children or in adolescents. Eight-week HIT had a small positive effect on executive functions measured by the trail making task in adolescents aged 15 years [12]. A single bout

*Correspondence address:* Eero Haapala, Sport and Exercise Medicine, University of Jyväskylä, Rautpohjankatu 8 (LL185), Jyväskylä, PL 35, 40014, Finland, e-mail: eero.a.haapala@ju.fi

Received: November 15, 2016

Accepted for publication: June 9, 2017

*Citation:* Stenman M, Pesola AJ, Laukkanen A, Haapala EA. Effects of two-week high-intensity interval training on cognition in adolescents – a randomized controlled pilot study. Hum Mov. 2017;18(2):15–20; doi: 10.1515/humo-2017-0019.

of HIT has also been linked to improved attention in 9–11-year-old children [13]. Furthermore, a single bout of HIT have been found to improve cognitive control in adults [14] and the results of some studies suggest positive effects of HIT on cognition and brain oxygenation [15, 16].

The aim of the study was to investigate the effects of a 2-week HIT on cognition in adolescents. We hypothesized that the adolescents in the exercise group would improve their cognition more than the adolescents in the control group.

## Methods

### Study design and participants

The study is based on data collected in the Neural Effects of Exercise, Diet, and Sleep (NEEDS) Study (ISRCTN12991197), pilot phase, 2015–2016. The participants were recruited from high schools located in the city of Jyväskylä, Finland, with an electronic messaging system used in these schools. The adolescents were eligible to participate in the study if they were apparently healthy and free of any cardiovascular disease, untreated or poorly controlled type 1 diabetes, musculoskeletal trauma or disorder, or severe depression or anxiety. The total of 25 adolescents volunteered to participate in the study. They were contacted by phone or by e-mail and then invited to the 1-hour baseline assessments on a convenient weekday during or after a school day in the exercise and health laboratory of the University of Jyväskylä. After the baseline assessments, the participants were allocated to either the intervention ( $n = 12$ ) or the control ( $n = 13$ ) group with the use of a computer-based randomizer ([www.randomizer.org](http://www.randomizer.org)). Altogether, 3 participants in the exercise group and 3 in the control group dropped out during the follow-up (Figure 1).

The protocol of the NEEDS Study was approved by the ethics committee of the University of Jyväskylä, Finland.

### Exercise intervention

The intervention included 4 running exercise sessions and 2 circuit training exercise sessions during a 2-week intervention period. Exercise sessions 1, 3, 4, and 6 were running sessions and exercise sessions 2 and 5 were circuit training sessions. All exercise sessions were separated by  $\geq 32$  hours. The exercise sessions were held during a school day at the school gymnasium, usually during the lunch break. The protocol of the running exercise sessions was adapted from Bond et al. [17]. The running protocol included a 3-minute standardized warm-up at light to moderate intensity. After the warm-up, the participants performed eight 1-minute maximal intensity sprint bouts, interspersed with 75-second pas-

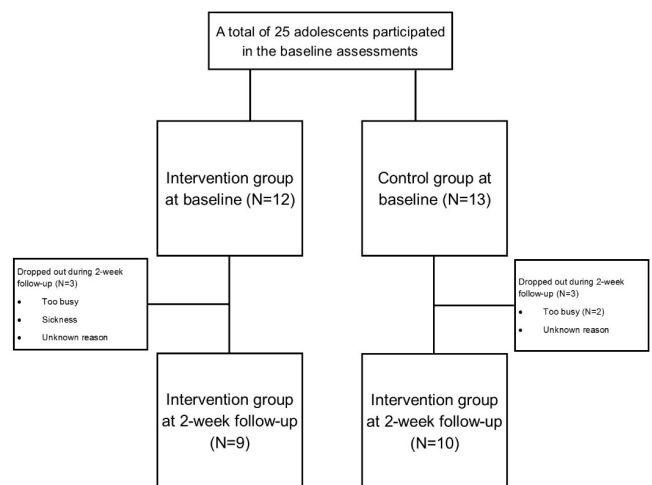


Figure 1. A flowchart of the NEEDS pilot study

sive or active recovery. Heart rate was monitored during each exercise session in randomly selected participants with the use of the Polar heart rate monitor (RS800CX, Polar Electro Ltd., Finland).

Circuit training was performed according to a modified Tabata protocol, which included 3 training sets. Each set comprised 2 different exercises activating large muscle groups (e.g. squat and running). The participants were asked to perform the first exercise for 20 seconds, rest for 10 seconds, perform the second exercise for 20 seconds, and rest for 10 seconds. This was continued until 4 rounds were completed. The second and the third training battery were performed with a similar work/rest ratio.

### Control group

The participants allocated to the control group were aware of the purpose of the study. However, they were not offered an intervention or instructions for PA but were encouraged to continue their usual daily habits.

### Assessments

All assessments were performed by trained research personnel. The baseline and follow-up assessments were carried out approximately at the same time of the day.

### Assessment of cognition

Cognition was assessed with the application of 5 different tasks from the computerized CogState battery (Cogstate Ltd, Melbourne, Australia). All tasks were instructed and explained by the assessor as recommended by the manufacturer. The tasks in the CogState battery were used to evaluate the key components of cognition and they are not influenced by differences in verbal skills or cultural background [18]. CogState battery has been reported to be a valid tool to assess neurocognitive func-

tioning in adolescents [19]. The results of the CogState battery correlate fairly well with the results of similar neurocognitive test batteries [20].

The processing speed was measured by the Detection Task (DET). The participants were asked to press a button as quickly as possible when a playing card flipped over on a computer screen. The score was the reaction time for correct responses ( $\log_{10}$  milliseconds), with a lower score indicating better performance.

Attention was measured by the Identification Task (IDT). In the IDT, the participants were asked to choose whether the card that flipped over was red or not. If the card was red, the participants were required to press 'yes,' and if the card was black, the participants were asked to press 'no'. The score was the reaction time for correct responses ( $\log_{10}$  milliseconds), with a lower score indicating better performance.

Working memory was assessed with the One Back Task (OBT) and the Two Back Task (TBT). In the OBT, the participants were instructed to decide, using buttons 'yes' or 'no,' whether a card presented was identical to the one presented just before. In the TBT, the participants were asked to choose whether a card presented was identical to the one presented two cards ago. The score in the OBT and TBT was the accuracy of the performance (arcsine transformation of the square root of the proportion of correct responses), with a higher score indicating better performance.

Visual learning and memory were evaluated by the Continuous Paired Association Learning Task (CPAL). First, the participants were instructed to learn and remember abstract pictures hidden beneath the circles in different locations on the computer screen. Second, the same abstract pictures were presented in the middle of the screen. The participants were instructed to recall where the same hidden pictures had been located. The score was the total number of errors, with a lower score indicating better performance.

#### Other assessments

Body height was measured twice with a wall mounted stadiometer, and the mean of these measurements was used in the analyses. Body weight, body fat mass, and fat free mass were evaluated with the InBody 720 bioimpedance device (InBody, Seoul, South Korea) after 3-hour fasting. Age- and sex-specific body mass index (BMI) for participants aged < 18 years were computed with the use of national reference values [21], and BMI for participants  $\geq 18$  years of age was calculated as body weight (kg)/(body height)<sup>2</sup> (m<sup>2</sup>). Pubertal status was assessed according to self-reported testicular development in boys and breast development in girls on the basis of the 5-stage criteria described by Tanner [22].

Cardiorespiratory fitness was evaluated by a maximal exercise test on an electromagnetically braked Monark

929E cycle ergometer (Monark Exercise AB, Sweden). The protocol included a 1-minute warm-up without resistance (workload 0) and an incremental exercise period with workload increasing by 1 watt/3 seconds until voluntary exhaustion. The participants were asked to keep the cadence of 70 during the test. The test was terminated when the participant was unable to keep the cadence of 50 or required to stop. The test was considered maximal if the reason to terminate it indicated maximal effort and cardiorespiratory capacity [23]. Cardiorespiratory fitness was defined as maximal workload at the end of the exercise test per fat free mass (W/FFM), derived from the bioimpedance analysis.

#### Statistical methods

We performed all data analyses using SPSS Statistics, version 21.0 (IBM Corp., Armonk, NY, USA). Basic characteristics were compared between the HIT and control groups with the Student's t-test and the chi-square test. The intervention effects on cognition were investigated with repeated measures analysis of variance. We also studied changes in the measures of cognition separately in the exercise group and the control group by the dependent samples t-test. Two sided *p*-values < 0.05 were considered statistically significant. We also evaluated the magnitude of changes in the measures of cognition, applying Morris  $d_{ppc2}$  as a measure of effect size (*ES*) [24]. Morris  $d_{ppc2}$  of 0.20 refers to a small, 0.50 to a moderate, and 0.80 to a large effect size [25].

## Results

#### Basic characteristics

The basic characteristics of the participants in the HIT and control groups are presented in Table 1. There were no differences in age, sex distribution, self-reported pubertal status, age- and sex-specific BMI, or BMI between the groups. The mean of the maximal heart rate during HIT was 195 (standard deviation [*SD*] = 6.0) and the mean heart rate during HIT was 175 (*SD* = 6.7). The HIT had a small to moderate effect on cardiorespiratory fitness (change in W/FFM in the intervention group = 0.49 vs. 0.28 in the control group,  $d_{ppc2}$  = 0.757).

We observed a statistically significant time\*group interaction effect on reaction time in the DET and IDT tasks (Table 2). Reaction times worsened in the HIT group but improved or remained stable in the control group. Further analyses confirmed these findings: the reaction time in the IDT was increased from baseline assessment to follow-up assessment in the HIT group ( $p$  = 0.020) but remained stable in the control group ( $p$  = 0.375). We also noted that while there was no change in the TBT response accuracy in the HIT group, the response accuracy improved in the control group (change in TBT accuracy: 0.03,  $p$  = 0.625 vs. 0.14,  $p$  = 0.01,  $d_{ppc2}$  = -0.47). The number of errors decreased significantly in the HIT

Table 1. Characteristics of the participants

	Intervention group ( <i>n</i> = 9)	Control group ( <i>n</i> = 10)	<i>p</i>
Age (years)	17.9 (0.9)	17.8 (0.7)	0.761
Gender distribution (girls/boys)	6/3	9/1	0.213
Self-reported pubertal status according to Tanner ( <i>n</i> )			0.360
I	0	0	
II	0	1	
III	2	0	
IV	3	4	
V	4	5	
Body height (cm)	170.9 (10.2)	166.5 (5.4)	0.249
Body weight (kg)	68.6 (11.8)	59.2 (6.4)	0.057
BMI	23.4 (2.0)	21.4 (2.3)	0.065
Body fat percentage (%)	22.6 (9.9)	21.5 (6.5)	0.770

## The effects of 2-week high-intensity interval training on cognition

group but no statistically significant change in the number of errors was observed in the control group (change:  $-35.8$ ,  $p = 0.039$  vs.  $-15.9$ ,  $p = 0.137$ ,  $d_{ppc2} = 0.419$ ).

### Discussion

In the presented study, we found that a 2-week HIT impaired processing speed and attention in adolescents. Furthermore, we observed that HIT had a small negative effect on working memory and a small positive effect on visual learning and memory. Despite the mixed effects of the HIT on cognition, the intervention also had a small to moderate impact on cardiorespiratory fitness.

Few studies have investigated the effects of HIT on cognition in children or adolescents. The only long term intervention study we are aware of observed moderate *ES* for the effects of 8-week HIT on executive function assessed by the trail making task [12]. Similarly, we found a moderate positive *ES* for visual memory and learning in favour of the intervention group. However, we also observed deteriorated reaction times among the HIT group, as well as improved working memory performance only in the control group. These results are in contrast with the outcomes obtained by Ma et al. [13], who noticed improved selective attention in children aged 9–11 years after a single bout of HIT. However, a direct comparison between studies in this field is difficult because the methods applied to assess cognition differ significantly. It is also possible that a simple reaction time task does not accurately reflect cognitive capacity among adolescents who are reaching their peak cognitive capacity. Furthermore, these few studies on the effects of HIT on cognition suggest that HIT may improve performance particularly in more complex cognitive tasks. This is in agreement with previous studies showing that exercise training has a pronounced effect on cognitive tasks requiring larger amount of cognitive control [26]. On the other hand, these studies may also

indicate that HIT has a relatively small impact on cognition. Furthermore, the intervention period in our study, as well as in the previous research, was relatively short in duration. It is possible that a longer HIT training period would have a stronger effect on cognitive functions.

Possible mechanisms how HIT may improve cognition include increased blood flow into the brain, increased synthesis of brain-derived growth factors, improved insulin sensitivity, and improved neural processing and synaptic plasticity [7, 15, 16, 27]. Furthermore, there are also possible mechanisms which may explain the decreased cognition in our study. High-intensity exercise has been found to increase oxidative stress and to decrease antioxidant capacity [28], which may have an adverse effect on brain and cognition [29]. Howard et al. also hypothesized that intense exercise might compromise the energy balance needed for brain growth and development [30]. Some evidence suggests that improved cardiorespiratory fitness is associated with better cognition in children [27]. Although we observed a larger improvement in cardiorespiratory fitness in the HIT group than in the control group, it is possible that these changes were not sufficient to elicit clear positive effects on cognition in our study group.

The strengths of the present study include the randomized controlled design and valid and objective measures of cognition and cardiorespiratory fitness. We also conducted the training sessions in a school setting, which increases the translatability of the results to everyday life. The main limitations of our study consist in a small sample size, as well as unequal number of boys and girls. The participants were also relatively lean and fit, which may hinder the effects of the HIT on cognition and cardiorespiratory fitness. Furthermore, the intervention lasted only for 2 weeks, and possibly a longer training period is required for larger effects.

In conclusion, the 2-week HIT had mixed effects on cognition in adolescents. Although already 2-week HIT

Table 2. The effects of 2-week high-intensity interval training (HIT) on cognition in adolescents

	HIT group (n = 9)			Control group (n = 10)			Repeated measures ANOVA		
	Baseline		Difference	Baseline		Difference	Time	Group	Time*group
	Mean (SD)	Follow-up Mean (SD)		Mean (SD)	Follow-up Mean (SD)				
Detection Task (reaction time)	2.48 (0.03)	2.47 (0.03)	0.10 (0.103)	2.588 (0.18)	2.54 (0.11)	-0.11 (0.11)	0.291	0.139	<b>0.025</b>
Identification Task (reaction time)	2.67 (0.05)	2.70 (0.05)	0.10 (0.103)	2.66 (0.04)	2.65 (0.03)	-0.10 (0.10)	0.234	0.111	<b>0.017</b>
One Back Task (accuracy)	1.32 (0.25)	1.42 (0.26)	0.11 (0.113)	1.30 (0.21)	1.33 (0.23)	0.10 (0.12)	0.552	0.831	0.821
Two Back Task (accuracy)	1.25 (0.26)	1.28 (0.29)	0.10 (0.112)	1.13 (0.20)	1.27 (0.27)	0.11 (0.12)	<b>0.023</b>	0.569	0.107
Continuous Paired Association Learning Task (errors)*	68.3 (61.2)	32.6 (44.8)	-35.2 (39.12)	42.1 (27.7)	26.2 (21.6)	-15.9 (35.1)	<b>0.004</b>	0.546	0.362

Bold indicates statistically significant effects from the repeated measures ANOVA.

has been found to efficiently improve cardiovascular health in youth [17], our results suggest that short term HIT may not be an optimal training mode to improve cognition in adolescents. However, these outcomes should be replicated and confirmed among larger study samples and with a longer training period.

#### Acknowledgements

This study was financially supported by the Päivikki and Sakari Sohlberg Foundation and the Jenny and Antti Wihuri Foundation.

#### References

- Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet*. 2012;380(9838):219–229; doi: 10.1016/S0140-6736(12)61031-9.
- Colley RC, Garriguet D, Janssen I, Craig CL, Clarke J, Tremblay MS. Physical activity of Canadian children and youth: accelerometer results from the 2007 to 2009 Canadian Health Measures Survey. *Health Rep*. 2011;22(1):15–23.
- Poitras VJ, Gray CE, Borghese MM, Carson V, Chaput JP, Janssen I, et al. Systematic review of the relationships between objectively measured physical activity and health indicators in school-aged children and youth. *Appl Physiol Nutr Metab*. 2016;41(6 Suppl 3):S197–S239; doi: 10.1139/apnm-2015-0663.
- Donnelly JE, Hillman CH, Castelli D, Etnier JL, Lee S, Tomporowski P, et al. Physical activity, fitness, cognitive function, and academic achievement in children: a systematic review. *Med Sci Sports Exerc*. 2016;48(6):1197–1222; doi: 10.1249/MSS.0000000000000901.
- Harris KC, Kuramoto LK, Schulzer M, Retallack JE. Effect of school-based physical activity interventions on body mass index in children: a meta-analysis. *CMAJ*. 2009;180(7):719–726; doi: 10.1503/cmaj.080966.
- Biddle SJH, Batterham AM. High-intensity interval exercise training for public health: a big HIT or shall we HIT it on the head? *Int J Behav Nutr Phys Act*. 2015;12(1):95; doi: 10.1186/s12966-015-0254-9.
- Metcalfe RS, Babraj JA, Fawcner SG, Volvaard NB. Towards the minimal amount of exercise for improving metabolic health: beneficial effects of reduced-exertion high-intensity interval training. *Eur J Appl Physiol*. 2012;112(7):2767–2775; doi: 10.1007/s00421-011-2254-z.
- Gillen JB, Gibala MJ. Is high-intensity interval training a time-efficient exercise strategy to improve health and fitness? *Appl Physiol Nutr Metab*. 2014;39(3):409–412; doi: 10.1139/apnm-2013-0187.
- Logan GR, Harris N, Duncan S, Schofield G. A review of adolescent high-intensity interval training. *Sport Med*. 2014;44(8):1071–1085; doi: 10.1007/s40279-014-0187-5.
- Kwak L, Kremers SP, Bergman P, Ruiz JR, Rizzo NS, Sjöström M. Associations between physical activity, fitness, and academic achievement. *J Pediatr*. 2009;155(6):914–918; doi: 10.1016/j.jpeds.2009.06.019.
- Esteban-Cornejo I, Tejero-Gonzalez CM, Sallis JF, Veiga OL. Physical activity and cognition in adolescents: a systematic review. *J Sci Med Sport*. 2015;18(5):534–539; doi: 10.1016/j.jsams.2014.07.007.

12. Costigan SA, Eather N, Plotnikoff RC, Hillman CH, Lubans DR. High-intensity interval training on cognitive and mental health in adolescents. *Med Sci Sports Exerc.* 2016;48(10):1985–1993; doi: 10.1249/MSS.0000000000000993.
13. Ma JK, Le Mare L, Gurd BJ. Four minutes of in-class high-intensity interval activity improves selective attention in 9- to 11-year olds. *Appl Physiol Nutr Metab.* 2015;40(3):238–244; doi: 10.1139/apnm-2014-0309.
14. Alves CR, Tessaro VH, Teixeira LA, Murakava K, Roschel H, Gualano B, et al. Influence of acute high-intensity aerobic interval exercise bout on selective attention and short-term memory tasks. *Percept Mot Skills.* 2014;118(1):63–72; doi: 10.2466/22.06.PMS.118k10w4.
15. Drigny J, Gremeaux V, Dupuy O, Gayda M, Bherer L, Juneau M, et al. Effect of interval training on cognitive functioning and cerebral oxygenation in obese patients: a pilot study. *J Rehabil Med.* 2014;46(10):1050–1054; doi: 10.2340/16501977-1905.
16. Lucas SJ, Cotter JD, Brassard P, Bailey DM. High-intensity interval exercise and cerebrovascular health: curiosity, cause, and consequence. *J Cereb Blood Flow Metab.* 2015;35(6):902–911; doi: 10.1038/jcbfm.2015.49.
17. Bond B, Cockcroft EJ, Williams CA, Harris S, Gates PE, Jackman SR, et al. Two weeks of high-intensity interval training improves novel but not traditional cardiovascular disease risk factors in adolescents. *Am J Physiol Heart Circ Physiol.* 2015;309(6):H1039–H1047; doi: 10.1152/ajpheart.00360.2015.
18. CogState. CogState Research. Melbourne: CogState Limited; 2001.
19. Dingwall KM, Lewis MS, Maruff P, Cairney S. Reliability of repeated cognitive testing in healthy Indigenous Australian adolescents. *Aust Psychol.* 2009;44(4):224–234.
20. Maruff P, Thomas E, Cysique L, Brew B, Collie A, Snyder P, et al. Validity of the CogState brief battery: relationship to standardized tests and sensitivity to cognitive impairment in mild traumatic brain injury, schizophrenia, and AIDS dementia complex. *Arch Clin Neuropsychol.* 2009;24(2):165–178; doi: 10.1093/arclin/acp010.
21. Saari A, Sankilampi U, Hannila ML, Kiviniemi V, Keseli K, Dunkel L. New Finnish growth references for children and adolescents aged 0 to 20 years: length/height-for-age, weight-for-length/height, and body mass index-for-age. *Ann Med.* 2011;43(3):235–248; doi: 10.3109/07853890.2010.515603.
22. Taylor SJ, Whincup PH, Hindmarsh PC, Lampe F, Odoiki K, Cook DG. Performance of a new pubertal self-assessment questionnaire: a preliminary study. *Paediatr Perinat Epidemiol.* 2001;15(1):88–94; doi: 10.1046/j.1365-3016.2001.00317.x.
23. Armstrong N, Welsman J, Winsley R. Is peak  $\text{VO}_2$  a maximal index of children's aerobic fitness? *Int J Sports Med.* 1996;17(5):356–359; doi: 10.1055/s-2007-972860.
24. Morris SB. Estimating effect sizes from pretest-posttest-control group designs. *Organ Res Methods.* 2008;11(2):364–386; doi: 10.1177/1094428106291059.
25. Cohen J. A power primer. *Psychol Bull.* 1992;112(1):155–159; doi: 10.1037/0033-2909.112.1.155.
26. Khan NA, Hillman CH. The relation of childhood physical activity and aerobic fitness to brain function and cognition: a review. *Pediatr Exerc Sci.* 2014;26(2):138–146; doi: 10.1123/pes.2013-0125.
27. Gomez-Pinilla F, Hillman C. The influence of exercise on cognitive abilities. *Compr Physiol.* 2013;3(1):403–428; doi: 10.1002/cphy.c110063.
28. Goto C, Higashi Y, Kimura M, Noma K, Hara K, Nakagawa K, et al. Effect of different intensities of exercise on endothelium-dependent vasodilation in humans: role of endothelium-dependent nitric oxide and oxidative stress. *Circulation.* 2003;108(5):530–535; doi: 10.1161/01.CIR.0000080893.55729.28.
29. Yirmiya R, Goshen I. Immune modulation of learning, memory, neural plasticity and neurogenesis. *Brain Behav Immun.* 2011;25(2):181–213; doi: 10.1016/j.bbi.2010.10.015.
30. Howard SJ, Cook CJ, Said-Mohamed R, Norris SA, Draper CE. The (possibly negative) effects of physical activity on executive functions: implications of the changing metabolic costs of brain development. *J Phys Act Health.* 2016;13(9):1017–1022; doi: 10.1123/jpah.2015-0687.