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9 **Title Page**

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11 **How physical activity, fitness and motor skills contribute to math** 12 **performance: Working memory as a mediating factor**

13

14 **Original Investigation**

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30 **Competing interests**

31 The authors declare no conflict of interest.

32 **Authors' contributions**

33 HJS and THT contributed to study design and recruitment. JK and HH conducted accelerometer-based
34 physical activity measurements and data analysis. LJ contributed to fitness measurements and VI and PR to
35 cognitive measurements. HJS and AK conducted statistical analysis and wrote the first draft of the
36 manuscript. CHH contributed to the manuscript with his expertise related to the topic. All authors
37 contributed to the interpretation of the results and helped to improve manuscript. All authors have read and
38 approved the final version of the manuscript.

39 **Availability of data**

40 The data that support the findings of this study are available on request from the corresponding author. The
41 data are not publicly available due to privacy or ethical restrictions.

42 **ABSTRACT**

43 **PURPOSE:** The purpose of this study was to examine whether physical activity, fitness and motor
44 skills have indirect association with math performance via cognitive outcomes and if so, through
45 which aspects of cognition? **METHODS:** This study comprised 311 6th–9th grade adolescents (12–
46 17y [M age=14.0y], 59% girls) from seven schools throughout Finland in 2015. Math performance
47 was measured via a teacher-rated math achievement and the Basic Arithmetic test. Cognitive
48 functions were measured by broad cognitive test battery. Physical activity was assessed with a
49 self-reported questionnaire and a hip-worn accelerometer. Aerobic fitness was estimated using a
50 maximal 20-m shuttle run test, muscular fitness with curl-up and push-up tests, and motor skills
51 with a 5-leaps test and a throwing-catching combination test. Structural equation modeling was
52 applied to examine the associations. **RESULTS:** In both boys and girls, motor skills had a positive
53 indirect association with math outcomes through visuospatial working memory. Among girls,
54 muscular fitness had a positive indirect association with math outcomes through visuospatial
55 working memory. Aerobic fitness was positively associated with math achievement, but the
56 indirect path via cognition was not observed. Self-reported physical activity had a borderline
57 indirect positive association with math outcomes through visuospatial working memory.
58 Accelerometer-based physical activity did not correlate with math performance. **CONCLUSION:**
59 Motor skills and muscular fitness had indirect, positive associations with math performance,
60 mediated by visuospatial working memory. The results give support to the viewpoints that the
61 connections between motor skills, fitness and physical activity to academic skills are mediated via
62 specific cognitive skills.

63

64 **Key words:** adolescents, motor skills, physical fitness, working memory

65

66 1 INTRODUCTION

67 Internationally, a lack of interest towards mathematics continues to rise.¹ Difficulties in math
68 learning are common, and for example two thirds of children in the United States have difficulties
69 to achieve the expected level of performance in both 4th and 8th grades.² Even in countries, where
70 overall achievement in mathematics are higher, 6% of children have mathematics learning
71 disabilities, and 26% have persistently low achievement in mathematics.³ Math skills are
72 considered to be crucial for success in Western societies, and severe numeracy difficulties may
73 have a serious impact on occupational and social opportunities.^{2,4}

74 Being physically active and fit is known to benefit brain health and function, and is
75 especially beneficial for cognitive function and academic performance.⁵ A growing body of
76 literature has shown positive associations of physical activity and fitness with math
77 performance.^{6,7} Further, the association between aerobic fitness and cognition, particularly
78 executive functions, has been found to be robust.⁵ However, less is known about the associations
79 of muscular fitness and motor skills with cognitive function and academic performance.⁸ Recently,
80 more attention has been focused on motor skills, since it has been suggested that coordinative,
81 cognitively engaging forms of exercise may also have effects on cognition along with less
82 cognitively engaging forms of exercise.^{9,10}

83 Executive function is defined as a group of higher-order cognitive processes involved in
84 self-regulatory and goal-directed actions, and is a strong predictor of academic performance.¹¹ In
85 particular, mathematics performance relies heavily on working memory, but also on other core
86 executive functions, such as inhibition and mental flexibility.⁴ Working memory is defined as the
87 ability to hold and manipulate information in mind; inhibition is defined as the ability to suppress
88 distracting information and unwanted responses; and mental flexibility refers to the ability to
89 flexibly shift between mental states, rule sets or tasks.¹¹ Furthermore, other aspects of cognition,
90 such as sustained attention and fluid reasoning (i.e., the ability to think logically and problem
91 solve in novel environments), which are associated with executive functions, have been shown to
92 relate to math performance.^{12,13} Likewise, visuo-spatial skills, especially spatial visualization, have
93 been found to both correlate and predict the development of math skills.¹⁴

94 It has been suggested that there is a need for further exploration of the mediators of
95 physical activity and academic performance.⁶ Many theories about underlying mechanisms have
96 been posited, for example biological and psychosocial theories as well as embodied learning
97 theories, which suggest that physical activity improves cognition via multiple, different pathways

98 and through that, academic performance.^{6,10} However, to date, the mediating role of cognitive
99 functions (mainly executive functions) between physical activity^{15,16}/ physical fitness^{17–19}/ motor
100 skills^{20,21}/ aerobic fitness^{22,23} and academic performance is not heavily studied. That is, only
101 couple of studies have assessed the mediating effects on mathematics.^{17,23,24}

102 The purpose of this study was to examine whether physical activity, fitness or motor skills
103 have indirect associations with mathematics performance through cognitive functions, and if so,
104 through which aspects of cognition? We hypothesized that physical activity, fitness and motor
105 skills are positively associated with cognitive functions and mathematics performance, and that the
106 association with mathematics are mediated by cognitive functions, with a particular focus on
107 executive functions.

110 2 METHODS

111 2.1 Study population

112 The participants were recruited in two waves. First, 805 students participating in a larger study
113 regarding the national “Finnish Schools on the Move” program were invited to participate in this
114 study during spring 2015.⁸ One hundred sixteen students from five schools with a wide
115 geographical representation of Finland participated in the study. Second, 484 students from two
116 schools in the Jyväskylä school district in Finland were invited to participate in this study during
117 autumn 2015, with 195 students agreeing to participate. Children, who needed specialized support
118 with individualized educational plan, were excluded from the analyses. Altogether, this study
119 comprised 311 6th–9th grade students (59% girls) from seven schools throughout Finland. Both the
120 students and their guardians gave written informed assent/consent to participate. The study
121 protocol was approved by the Ethics Committee of the University of Jyväskylä.

123 2.2 Math performance

124 The math performance was assessed from two different perspectives. The education services
125 provided students’ math achievements from the register. The scale for this teacher-rated numerical
126 evaluation was 4–10, where four denotes failure and 10 denotes excellent knowledge and skills.
127 This comprehensive evaluation is based on teacher’s continuous monitoring of the classroom
128 behaviour and multiple curriculum-based exams, and it tries to catch the overall level of the
129 mathematical skills in various types of curriculum-based math contents. Basic arithmetic skills

were determined with the Basic Arithmetic Test,²⁵ including addition, subtraction, multiplication and division tasks. Students were asked to perform as many problems as possible within a 3-minute time limit. The number of correct answers were used to illustrate arithmetic skills. This test measures the basic skills learned at the early grades. In addition, it measures rapid retrieval of facts and mental calculations algorithms from long-term memory. The test was conducted in a quiet group session under the guidance of two educated research personnel.

136

137 **2.3 Cognitive functions**

138 A battery of cognitive functions was measured, which included a modified flanker task, four tests
139 (Paired Associates Learning (PAL), Spatial Working Memory (SWM), Reaction Time (RTI) and
140 Rapid Visual Information Processing (RVP)) from the Cambridge Neuropsychological Test
141 Automated Battery (CANTAB) (CANTAB eclipse version 6, Cambridge Cognition, Cambridge,
142 UK), four tests, one from each main indexes (Similarities, Matrix Reasoning, Digit Span, and
143 Coding) from the Wechsler Intelligence Scale for Children (WISC-IV), and the Spatial Relations
144 subtest from the Woodcock-Johnson test battery. The modified flanker task and CANTAB tests
145 were assessed with tablets (Dell Venue 11 Pro 7130, screen 10.8", processor: Intel® Core™ i5-
146 4300Y CPU 1.60 GHz, Memory (RAM): 4.00 GB, System type: 64-bit, x64-based processor),
147 while WISC tests and Spatial Relations subtest were measured with pen and paper. A flanker task,
148 four CANTAB tests, and two WISC tests (Similarities and Digit Span) were run individually in a
149 sound-attenuated location with the guidance of trained research assistants and in accordance with
150 the standard instructions. The test battery took about 45 minutes to complete. The Spatial
151 Relations subtest and two WISC tests (Coding and Matrix Reasoning) were assessed together with
152 the arithmetic test in a small group session under the supervision of two trained research assistants.
153 This session took about 30 minutes to complete.

154 A modified version of the Eriksen flanker task²⁶ was used to assess attentional inhibition.
155 From the CANTAB test battery, the PAL test assessed visual memory, the SWM test assessed
156 visuospatial working memory, the RTI test assessed reaction and movement times to visual
157 stimulus, and the RVP test assessed sustained attention. Due to several variables produced by the
158 flanker task and each CANTAB tests, the principal component analysis (according to Rovio et
159 al.²⁷) was conducted separately for each individual test to reduce the number of variables and to
160 identify components accounting for most of the variation within the cognition data set. The
161 weights for the observed items of the cognitive tests used to create the principal components are

presented in Supporting information table S1. Each component represented the performance in a particular cognitive test and were normalized based on the rank order normalization procedure, producing variables with mean value of 0 and a standard deviation of 1.

From the WISC test battery, the Similarities test assessed verbal concept formation and verbal abstract reasoning, the Matrix Reasoning test assessed fluid reasoning, the Digit Span test assessed auditory verbal working memory and the Coding test assessed processing speed. For each of these WISC tests, the number of correct answers (raw scores of standardized scores) were calculated to represent performance. The Spatial Relations subtest is a subtest from the Woodcock and Johnson²⁸ test battery measuring spatial visualization ability. The number of correctly solved items within three-minute time limit was calculated to represent spatial visualization ability. The cognitive tests are described in more detail in 1.1 Cognitive functions in Supporting information file.

2.4 Physical activity

Physical activity was self-reported by a questionnaire and measured by a hip-worn accelerometer. Self-reported physical activity was assessed with the question used in Health Behaviour in School-aged Children survey.²⁹ The question assessed self-reported physical activity with moderate-to-vigorous intensity by asking how many days participants were physically active for a total of at least 60 minutes per day during a typical week. The response categories were as follows: 0 days, 1 day, 2 days, ...7 days. A short description of moderate-to-vigorous physical activity (MVPA) and examples assisted in answering the question. Accelerometer-based physical activity was measured with GT3X+ and wGT3X+ accelerometers (Pensacola, Florida, USA) worn on the right hip during waking hours for seven full, consecutive days. Bathing or other water-based activities were excluded. Data were collected in raw 30 Hz acceleration standardly filtered and converted into 15-s epoch counts. Data reduction was made with a customized Visual Basic macro for Excel software. For a valid monitoring period, readings including at least 500 min/day measured between 7:00 am and 11:00 pm on three days were required.³⁰ Non-wear time was defined as periods of 30 min of consecutive zero counts and spurious accelerations (over 20,000 counts per minute (cpm)) were ruled out.³¹ Participants' average device wearing time was 782 min (SD=49) per day. Evenson et al.'s³² cut-points were used to calculate MVPA (≥ 2296 cpm).

2.5 Physical fitness and motor skills

194 Aerobic fitness, muscular fitness and motor skills were measured in small group sessions with the
195 tests included in the Move! - monitoring system for physical functional capacity.³³ Aerobic fitness
196 was estimated with a 20-m shuttle run test, where running speed was gradually increased with 1-
197 minute intervals until maximal voluntary exhaustion. Results of the test were the number of laps
198 run. Muscular fitness was determined via the sum of abdominal and upper-body muscle strength.
199 Abdominal strength was measured with a curl-up test, where the number of curl-ups performed
200 (maximal number of repetitions limited to 75) was calculated as the test result. Upper-body muscle
201 strength was measured with a push-up test with slightly different technique for boys and girls;
202 boys had hands and toes on the ground and girls had hands and knees on the ground. The test
203 result was the number of push-ups performed during a 1-minute period. Motor skills were
204 determined via the sum of the performance in a 5-leaps test and a throwing-catching combination
205 test. In the 5-leaps test, students performed five consecutive leaps with the instruction to jump as
206 far as they can. The test result was the length of the performance recorded with 0.1 m accuracy. In
207 the throwing-catching combination test, students performed an overhand throw of a tennis ball
208 from a set distance to a target placed on the wall and then caught the ball after one bounce. The
209 test result was the number of correctly performed attempts out of 20. All results of the tests were
210 standardized according to sex and age group. The measurements are described in more detail in
211 the study of Joensuu et al.³³

212

213 **2.6 Confounding factors**

214 Pubertal stage was assessed via a self-assessment questionnaire answered by students and
215 categorized according to the Tanner puberty stage.³⁴ Body fat percentage was measured via body
216 composition analyzer InBody 720. Students' learning difficulties and mother's education were
217 assessed via a web-based survey completed by a parent or guardian. The questions were as
218 follows: "Does your child have any diagnosed learning difficulties?" (categorization, yes (1) and
219 no (0)). "What is the level of mother's education?" (categorization, tertiary level education (1) and
220 basic or upper secondary education (0)).

221

222 **2.7 Statistical analysis**

223 The descriptive statistics were calculated by using SPSS 25.0 for Windows (SPSS Inc., Chicago,
224 IL, USA), and all further analyses were conducted using Mplus statistical package (Version 7, Los
225 Angeles, CA, USA).³⁵ The descriptive statistics are presented as means and standard deviations or

percentages (%). Differences in the study variables between girls and boys were tested via Student's t-test or Pearson's chi-squared test. As preliminary analysis, the sample correlation coefficients among the study variables were estimated among all and separately among boys and girls.

To study associations of physical activity/fitness/motor skills on cognitive functions and math performance, as well as the mediating role of cognitive function in the relationship between physical activity/fitness/motor skills and math performance, path modeling within structural equation modeling framework was utilized. All regressions were adjusted for potential confounding variables, including age, sex, pubertal stage, body fat percentage, learning difficulties and mother's education. First, the direct associations of physical activity/fitness/motor skills on cognitive function/math performance were modelled by using linear regression. Second, a mediator model, including one cognitive function as a mediator at a time, was estimated (see Figure 1). The model included indirect paths from physical activity/fitness/motor skills to both outcomes of math performance (arithmetic skills and teacher-rated math performance) through a cognitive test. The math performance outcomes were allowed to correlate.

The Satorra-Bentler scaled χ^2 -test, the comparative fit index (CFI), the Tucker-Lewis Index (TLI), the root mean square error of approximation (RMSEA), and the standardized root-mean-square residual (SRMR) were used to evaluate the goodness-of-fit of the models. The model fits the data well if the P-value for the χ^2 -test is non-significant, CFI and TLI values are close to 0.95, the RMSEA value is below 0.06, and the SRMR value is below 0.08 (Hu & Bentler 1999). If the model did not fit the data adequately well, the direct effects from physical activity/fitness/motor skills to math score or teacher-rated math performance were additionally estimated. Indirect effects of interest were calculated as a product of the regression coefficients ($a \times b1$, $a \times b2$) and tested for significance. When the interaction term [physical activity/fitness/motor skills \times gender (girl)] was needed to add in the model, the indirect effects were calculated separately for girls and boys by using the parameters of the model (boys: $a \times b1$, $a \times b2$; girls: $(a+i1) \times b1$, $(a+i1) \times b2$). To control for Type 1 error rate the significance level of the study was set at 0.01.

More information about linear regression models and technical details of the modeling are provided in the Supporting information file (see 1.2.1 Linear regression models and 1.2.2 Technical details of the modeling).

258 3 RESULTS

259
260 Sex-specific distributions and gender differences in observed variables are presented in Table 1.

261

262 3.1 Mediator models

263 Because accelerometer-based PA did not correlate with math performance, no further modeling
264 was conducted. In addition, performance on the RTI test did not correlate with math performance,
265 and the association of Digit span with math performance was attenuated after adjusting for
266 confounding variables. Therefore, these cognitive functions were not considered as mediating
267 variables in the modeling.

268 The mediator models including only the indirect associations of self-reported PA on math
269 performance through a cognitive outcome (SWM, RVP, Matrix reasoning and Coding test) fitted
270 the data well, indicating that the association was fully mediated through each cognitive function
271 (see Table S6). The mediator models for aerobic fitness (SWM and Similarities test as mediators),
272 muscular fitness (flanker task, SWM, RVP and Spatial relations tests as mediators) and motor
273 skills (flanker task, PAL, SWM, RVP, Similarities, Matrix reasoning and Spatial relations test)
274 including only the indirect effects did not fit the data adequately well, and therefore the direct
275 effects from aerobic fitness on math performance were additionally estimated (see Table S6).

276 The estimation results of the mediator models are presented in Table 2 and Table 3 (see
277 also Figure 1).

278

279 3.2 Indirect associations

280 The estimated unstandardized indirect associations are presented in Tables 4 and 5. Of the
281 cognitive outcomes, which were associated with both math performance and physical
282 activity/fitness/motor skills, SWM mediated the associations of muscular fitness and motor skills
283 with math performance at a significance level of 0.01. Muscular fitness had a positive indirect
284 association with both teacher-rated math achievement and arithmetic skills through performance in
285 the SWM test among girls (unstandardized indirect association $b=0.06$, $p=0.003$; $b=0.17$, $p=0.003$,
286 respectively). In addition, motor skills had a positive indirect association with both teacher-rated
287 math achievement and arithmetic skills through performance in the SWM test among all children
288 ($b=0.07$, $p=0.001$; $b=0.19$, $p<0.001$, respectively).

Several cognitive functions appeared to mediate the associations at the significance level of 0.05 but these associations did not reach significance at the 0.01 level. Self-reported physical activity had a positive indirect association with both teacher-rated math achievement and arithmetic skills through performance in the SWM test among all children ($b=0.04, p=0.014$; $b=0.10, p=0.016$, respectively). In addition, among boys, self-reported physical activity had a positive indirect association with both teacher-rated math achievement and arithmetic skills through performance in the RVP test ($b=0.07, p=0.022$; $b=0.23, p=0.021$, respectively) and Matrix reasoning test ($b=0.06, p=0.043$; $b=0.13, p=0.036$, respectively).

Aerobic fitness had a negative indirect association with teacher-rated math performance through performance in the Similarities test among boys ($b=-0.08, p=0.047$). Muscular fitness had a positive indirect association with both teacher-rated math achievement and arithmetic skills through performance in the RVP test among all children ($b=0.04, p=0.043$; $b=0.14, p=0.047$, respectively).

Motor skills had a positive indirect association with both teacher-rated math achievement and arithmetic skills through performance RVP test ($b=0.04, p=0.023$; $b=0.13, p=0.023$, respectively) and Matrix reasoning test ($b=0.04, p=0.038$; $b=0.11, p=0.042$, respectively) among all children. In addition, motor skills had a positive indirect association with arithmetic skills through performance on the flanker task ($b=0.09, p=0.023$) and PAL test ($b=0.07, p=0.046$) as well as with teacher-rated math achievement through performance in the Spatial relations test ($b=0.04, p=0.030$). Furthermore, among boys, motor skills had a negative indirect association of with both arithmetic skills and teacher-rated math achievement through performance on the Similarities test ($b=-0.06, p=0.017$; $b=-0.17, p=0.020$, respectively).

3.3 Supporting results

The correlation coefficients for study variables among all children are presented in the supporting Table S2 and separately for boys and girls in the supporting Table S3. The estimation results of the linear regression models for the direct associations of physical activity, fitness and motors skills with cognitive and math outcomes are presented in the supporting information file (the chapter 2.1 Direct associations) and Tables S4 and S5. These associations were adjusted for age, sex, pubertal stage, body fat percentage, learning difficulties and mother's education. The model-fit of the mediator models are presented in supporting Table S6.

321

322 **4 DISCUSSION**

323 **4.1 Main findings**

324 This study examined whether physical activity, fitness or motor skills have indirect associations
325 with mathematics performance through cognitive functions, and if so, through which aspects of
326 cognition. The present results indicate that muscular fitness and motor skills had a positive indirect
327 association with math achievement and arithmetic skills through visuospatial working memory. In
328 addition, several other cognitive functions (e.g. sustained attention and fluid reasoning) appeared
329 to mediate the associations at the significance level of 0.05, but these associations did not reach
330 significance at the 0.01 level.

331

332 **4.2 Visuospatial working memory mediating the associations of muscular fitness and motor** 333 **skills with math performance**

334 The results of this study replicate earlier findings indicating that cognitive functions play a role in
335 mediating the association between physical activity, fitness and motor skills with academic
336 achievement.^{15,17–21} This study adds value to the existing literature by showing that visuospatial
337 working memory were the strongest cognitive function mediating the associations of muscular
338 fitness and motor skills with math performance. In addition, even though, different aspects of math
339 performance were assessed, the indirect paths between muscular fitness/motor skills and
340 mathematics via working memory were quite similar.

341 **4.2.1 Working memory**

342 Previous studies examining the association between math performance and executive functions
343 have suggested that among all core executive functions, working memory has the strongest
344 association with mathematical performance, while the roles of inhibition and shifting are less
345 studied and the findings have been mixed.⁴ Earlier studies have also suggested that working
346 memory may play a role as a mediator between physical fitness and academic outcomes more
347 often than the other core executive components. De Bruijn et al.¹⁷ showed that working memory
348 mediated the association between physical fitness (a component score of aerobic fitness, muscular
349 strength, running speed and agility and upper-limb agility) and mathematics in eight-year-old
350 children, while inhibition or mental flexibility did not. We replicated these results by showing that,
351 from the executive outcomes assessed, visuospatial working memory, mediated the positive
352 association of muscular fitness and motor skills with mathematics. Furthermore, Núñez et al.²³

showed that inhibition did not mediate the relationship between aerobic fitness and math fluency, a finding supported herein.

In the study of De Bruijn et al.¹⁷, both verbal and visuospatial working memory performance mediated the association of physical fitness and mathematics. In this study, verbal working memory did not have an association with any physical activity, fitness or motor skills measures (see Table S2), while visuospatial working memory mediated the positive association of muscular fitness and motor skills with mathematics. The present results highlight the role of visuospatial working memory as the mediator between physical activity/fitness/motor skills and mathematics. This might result from the requirements of physical activity/fitness/motor skills components; the ability to process and manipulate visuospatial information is routinely needed when being physically active or performing complex motor skill tasks.

4.2.2 Other aspects of cognition

From the other measured aspects of cognition, sustained attention and fluid reasoning appeared to systematically mediate the indirect associations of self-reported physical activity/muscular fitness/motor skills and math performance at the significance level of 0.05. It seems that, besides working memory, there may be other cognitive functions that may mediate the association of physical activity/fitness/motor skills and math performance. Attentional performance has been related to academic success in mathematics,¹² while fluid reasoning has shown to be important predictor of future math achievement in childhood and adolescence,¹³ and explain the development of arithmetic skills.³ Even though, visuospatial working memory, sustained attention and fluid reasoning are highly correlated, they may have unique contributions to math achievement, which may explain the borderline indirect associations observed.

4.3 Associations of physical activity, fitness and motor skills with math performance

In most previous studies, where cognition mediated the association of fitness and academic achievement, physical fitness components included aerobic, muscular and motor skill specific fitness measures.¹⁷⁻¹⁹ In this study, we wanted to examine these different components separately. Of the measured variables, muscular fitness and motor skills had an indirect association with math performance through cognition. Further, in this study, motor skills were the most systematically associated with academic and cognitive performance. Moreover, even though aerobic fitness had direct positive associations with math and cognitive performance, the indirect path to math via cognition was not observed. Self-reported physical activity was associated with cognitive and

385 math performance and had a borderline positive indirect association with math performance via
386 visuospatial working memory. Accelerometer-based physical activity was not associated with
387 math performance, replicating the results of earlier studies.^{7,8,36} The inconsistency between
388 physical activity measures may occur because the measures reflect different contents and
389 constructs of physical activity.³⁶

390 The present results partially replicate those of Schmidt et al.²¹, who showed that motor
391 coordination had an indirect association with academic achievement through executive functions.
392 However, aerobic and muscular fitness did not exhibit a similar indirect association.²¹ Cadoret et
393 al.²⁰ showed that motor skills had a positive effect on academic achievement through an indirect
394 path via cognitive ability. Whereas, Núñez et al.²³ showed that the relationship between aerobic
395 fitness and math fluency was not mediated by inhibition. Similarly, Aadland et al.²⁴ showed that
396 executive functions did not mediate the associations of accelerometer-based physical activity and
397 aerobic fitness with academic achievement, while the association between motor skills and
398 academic performance seemed to be modestly mediated by executive functions. On the contrary,
399 in the study of Visier-Alfonso et al.²², aerobic fitness had an indirect association with academic
400 achievement through inhibition and cognitive flexibility. As such, the effects of motor skills on
401 academic success appear to be mediated more often by cognition, while the effects of aerobic
402 fitness on academic achievement appear to be mediated by other factors, such as molecular and
403 cellular mediators, structural and functional brain changes and behavioral and socioemotional
404 mediators.³⁷

405 The systematic associations of motor skills with cognitive and math outcomes, and the
406 mediating role of cognitive functions between motor skills and mathematics, may be due to that
407 motor and cognitive skills are developmentally linked.^{38,39} Especially, the higher-order cognitive
408 skills are needed to perform complex motor skills, which is supported by the co-activation of the
409 cerebellum and the prefrontal cortex, the brain areas important for complex and coordinated
410 movements and higher-order cognitive skills, respectively.³⁸ Intervention studies on improving
411 motor coordination could be one method to further explore this relationships between motor skills,
412 working memory and mathematics. To conclude the present results, the mediating role of
413 cognitive functions do not appear to be generalized, but rather more specific depending on
414 physical activity/fitness/motor skills dimensions measured and the academic outcomes used.

415

416 **4.4 Strengths and limitations**

417 To our knowledge, this is the first study identifying the cognitive functions mediating the
418 associations between physical activity/fitness/motor skills and math performance, including not
419 only executive outcomes, but also other aspects of cognition. Further, we used a relatively large
420 range measures of physical activity, fitness and motor skills instead of a combined fitness
421 outcome. Moreover, several important confounding factors were considered, and a comprehensive
422 analytical approach employing structural equation modelling was used. The major limitation
423 herein was the cross-sectional nature of the study, and there remains a need for intervention
424 studies to confirm these results. In addition, the participation rate in the first five schools of
425 recruitment was low because these students had been involved in a larger study for two years and
426 did not want to participate in additional measurements. For that reason, two new schools were
427 recruited, and the participation rates were adequate in those schools. Furthermore, the sample size
428 is small for the number of cognitive assessments and therefore, the statistical power to detect
429 small-sized indirect associations may be insufficient. To decrease the probability of a Type I error
430 due to multiple tests, we used a more stringent alpha level ($\alpha = 0.01$) for interpretation of the
431 results. Several cognitive outcomes mediated the associations at the alpha level of 0.05, but not at
432 0.01. Studies with larger sample sizes are required to verify these indirect associations. Lastly,
433 physical fitness and maturation were estimated, rather than directly measured, which may partly
434 explain the results.

435

436 **4.5 Perspective**

437 Physical activity and fitness are known to benefit cognitive function and academic performance.⁵
438 Since the need for clarifying the mediators between physical activity and academic performance
439 has been acknowledged⁶, the results of this study provide important novel information on the
440 mediating role of spatial working memory between the positive associations of muscular fitness,
441 motor skills and math performance. The mediating role of cognitive functions appear to be
442 specific depending on physical activity, fitness or motor skills dimensions measured, and which
443 academic outcomes assessed. Furthermore, this study showed that motor skills were the most
444 systematically associated with academic and cognitive performance, which suggests that physical
445 activity including not only aerobic, but also muscular and motor specific domains may benefit
446 math performance.

447

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Table 1. Sex-specific distributions and gender differences in observed variables

	All (N=310)			Boys (N=127)		Girls (N=183)		<i>p</i>
	N	Mean (SD)	Min, Max	N	Mean (SD)	N	Mean (SD)	
Age (years)	310	14.0 (1.1)	12, 17	127	14.1 (1.1)	183	14.0 (1.1)	0.378
Pubertal stage ^a	296	3.4 (0.9)	1, 5	123	3.5 (1.0)	173	3.3 (0.8)	0.031*
Math Performance								
Teacher-rated math ^b	308	8.2 (1.2)	4, 10	126	8.1 (1.1)	182	8.2 (1.2)	0.470
Arithmetic skills ^c	304	14.3 (3.6)	4, 24	123	15.0 (3.6)	181	13.9 (3.6)	0.011*
Cognitive functions								
Inhibition (component) ^d	297	0.0 (1.0)	-3.5, 1.8	122	-0.1 (1.2)	175	0.1 (0.9)	0.041*
Visual memory (component) ^e	305	2.9 (1.0)	-1.3, 4.2	124	2.8 (1.1)	181	3.0 (0.9)	0.086
Visuospatial working memory (component) ^f	305	1.5 (1.0)	-2.1, 3.6	124	1.6 (0.9)	181	1.4 (1.0)	0.105
Attentional reaction time (component) ^g	306	0.0 (1.0)	-3.0, 3.4	125	-0.3 (1.0)	181	0.2 (0.9)	<0.001***
Sustained attention (component) ^h	305	0.0 (1.0)	-4.0, 2.5	125	0.0 (1.1)	180	0.0 (0.9)	0.724
Verbal reasoning ⁱ	305	29.0 (4.0)	16, 37	125	28.7 (4.1)	180	29.2 (3.9)	0.260
Fluid reasoning ^j	304	26.3 (3.4)	14, 34	124	26.2 (3.6)	180	26.4 (3.3)	0.585
Auditory verbal working memory ^k	305	15.3 (2.9)	10, 25	125	15.3 (3.0)	180	15.3 (2.9)	0.961
Processing speed ^l	304	58.7 (13.5)	28, 99	124	56.7 (13.1)	180	60.1 (13.7)	0.033*
Spatial visualization ^m	304	21.4 (2.7)	9, 28	123	21.3 (2.6)	181	21.5 (2.8)	0.444
Physical activity								
Self-reported PA ⁿ	305	4.7 (1.9)	0, 7	124	5.0 (1.9)	181	4.4 (1.9)	0.018*
Accelerometer-based PA ^o	237	47.9 (21.0)	13.9, 133.2	86	54.1 (22.8)	151	44.4 (19.1)	0.001**
Fitness								
Aerobic fitness (standardized) ^p	268	0.0 (1.0)	-2.5, 2.3	112	0.0 (1.0)	156	0.0 (1.0)	0.988
Aerobic fitness ^q	268	49.0 (20.8)		112	58.9 (21.3)	156	41.9 (17.2)	<0.001***
Muscular fitness (standardized) ^r	264	0.0 (1.7)	-3.7, 4.5	109	0.0 (1.7)	155	0.0 (1.7)	0.867
Abdominal strength ^s	280	45.9 (22.8)		117	51.7 (23.0)	163	41.7 (21.8)	<0.001***
Upper-body muscle strength ^t	270	25.8 (13.4)		112	23.6 (13.8)	158	27.5 (12.9)	0.018*
Motor skills (standardized) ^u	276	0.0 (1.7)	-5.5, 3.4	114	0.0 (1.7)	162	0.0 (1.6)	0.979
Locomotor skills (a 5-leaps test) ^v	279	9.2 (1.2)		115	9.7 (1.3)	164	8.9 (1.0)	<0.001***
Manipulative skills (a throwing-catching combination test) ^w	286	12.9 (4.8)		118	14.0 (4.7)	168	12.2 (4.8)	0.002**
Body fat percentage (%) ^x	295	19.0 (8.3)	3.0, 49.8	122	13.8 (6.8)	173	22.6 (7.2)	<0.001***
Learning difficulties (yes) ^y	220	6.4 %		93	8.6 %	127	4.7 %	0.244
Mother education (tertiary level education) ^z	222	83.8 %		97	84.5 %	125	83.2 %	0.789

P value for gender differences (Student's *t*-test or Pearson's chi-squared test), **p* < 0.05, ***p* < 0.01, ****p* < 0.001.

^a Pubertal stage, based on self-assessment questionnaire and categorized according to the Tanner puberty stage, range 1–5.

^b Teacher-rated math achievement (a scale of 4–10, where 4 denotes a failure and 10 denotes excellent knowledge and skills).

^c Arithmetic skills, the Basic Arithmetic Test including addition, subtraction, multiplication and division tasks, the number of correct answers

^d Inhibition, a modified flanker task (the component score formed from response accuracy (%) and reaction time for correct answers (ms) for congruent and incongruent trials, and the interference score for response accuracy (congruent – incongruent))

- ^e Visual memory, the Paired Associates Learning (PAL) test from the CANTAB test battery (the component score formed from PAL First trial memory score, PAL Mean errors to success, PAL Mean trials to success, PAL Number of patterns succeeded on, PAL Stages completed, PAL Stages completed on first trial, PAL Total errors, PAL Total errors (adjusted), PAL Total trials, PAL Total trials (adjusted), PAL Total errors (6 shapes, adjusted) and PAL Total errors (8 shapes, adjusted))
- ^f Visuospatial working memory, Spatial Working Memory (SWM) test from the CANTAB test battery (the component score formed from SWM Between errors, SWM Between errors (4 boxes), SWM Within errors, SWM Within errors (4 boxes), SWM Total errors, SWM Total errors (4 boxes), SWM Strategy, SWM Mean time to first response, SWM Mean time to last response and SWM Mean token-search preparation time)
- ^g Attentional reaction time, Reaction Time (RTI) test from the CANTAB test battery (the component score formed from RTI Mean simple reaction time, RTI Mean simple movement time, RTI Simple accuracy score, RTI Simple error score (all), RTI Mean five-choice reaction time, RTI Mean five-choice movement time and RTI Five-choice accuracy score)
- ^h Sustained attention, Rapid Visual Information Processing (RVP) tests from the CANTAB test battery (the component score formed from RVP A', RVP B", RVP Probability of false alarm, RVP Probability of hit, RVP Mean latency, RVP Total correct rejections, RVP Total false alarms, RVP Total hits, RVP Total misses)
- ⁱ Verbal reasoning, Similarities test from the WISC test battery (the number of correct answers (raw scores))
- ^j Fluid reasoning, Matrix reasoning test from the WISC test battery (the number of correct answers (raw scores))
- ^k Auditory verbal working memory, Digit Span test from the WISC test battery (the component score formed from the raw scores for digit span forward and backward)
- ^l Processing speed, Coding test from the WISC test battery (the number of correct answers (raw scores))
- ^m Spatial visualization, Spatial relations test from the Woodcock-Johnson test battery (The number of correctly solved items)
- ⁿ Self-reported physical activity, how many days children were physically active for a total of at least 60 minutes per day with moderate-to-vigorous intensity during a typical or usual week. The response categories were as follows: 1= 0 days, 2 = 1 day, 3= 2 days, ...8 = 7 days
- ^o Accelerometer-based physical activity, measured with the ActiGraph accelerometer using a cut-off value 2296 counts per minute indicating moderate-to-vigorous intensity physical activity.
- ^p Aerobic fitness, standardized according to sex and age group
- ^q Aerobic fitness, a maximal 20-m shuttle run test (the number of laps run).
- ^r Muscular fitness, the sum of abdominal and upper-body muscle strength standardized according to sex and age group
- ^s Abdominal strength, a curl-up test (the number of curl-ups performed).
- ^t Upper-body muscle strength, a push-up test (the number of push-ups performed).
- ^u Motor skills, the sum of the locomotor skills and manipulative skills standardized according to sex and age group
- ^v Locomotor skills, a 5-leaps test (the length of the performance (m)).
- ^w Manipulative skills, a throwing-catching combination test (the number of correctly performed attempts).
- ^x Body fat percentage (%), measured via body composition analyser InBody 720.
- ^y Learning difficulties, asked from the main caregiver: Does your child have any diagnosed learning difficulties?" (categorization, yes (1) and no (0))
- ^z Mother's education, asked from the main caregiver: "What is the level of mother's education?" (categorization, tertiary level education (1) and basic or upper secondary education (0)).

Table 2. The estimation results of the mediator models of physical activity/fitness/motor skills on math performance through a computer-assisted cognitive function test.

	Flanker			PAL			SWM			RVP		
	<i>B</i>	<i>SE</i>	<i>p</i>	<i>B</i>	<i>SE</i>	<i>p</i>	<i>B</i>	<i>SE</i>	<i>p</i>	<i>B</i>	<i>SE</i>	<i>p</i>
Self-reported PA → Cognitive function → Math performance												
<i>Cognitive function</i>	- ^a			- ^a								
Self-reported PA, <i>a</i>							0.17	0.06	0.004*	0.24	0.10	0.016
Self-reported PA × gender (girl), <i>i1</i>							- ^b			-0.43	0.19	0.024
<i>Arithmetic skills</i>												
Cognitive function, <i>b1</i>							0.30	0.06	<0.001**	0.49	0.04	<0.001**
<i>Teacher-rated math</i>												
Cognitive function, <i>b2</i>							0.34	0.06	<0.001**	0.48	0.04	<0.001**
Muscular fitness → Cognitive function → Math performance												
<i>Cognitive function</i>				- ^a								
Muscular fitness, <i>a</i>	0.11	0.06	0.050				0.03	0.09	0.788	0.13	0.07	0.048
Muscular fitness × gender (girl), <i>i1</i>	- ^b						0.21	0.10	0.029	- ^b		
<i>Arithmetic skills</i>												
Cognitive function, <i>b1</i>	0.30	0.06	<0.001**				0.28	0.06	<0.001**	0.49	0.05	<0.001**
Muscular fitness, <i>c1</i>	0.09	0.07	0.158				-0.07	0.09	0.478	0.05	0.06	0.311
Muscular fitness × gender (girl), <i>i2</i>	- ^b						0.17	0.09	0.062			
<i>Teacher-rated math</i>												
Cognitive function, <i>b2</i>	0.16	0.06	0.012				0.28	0.06	<0.001**	0.37	0.06	<0.001**
Muscular fitness, <i>c2</i>	0.26	0.07	<0.001**				0.06	0.10	0.523	0.12	0.09	0.171
Muscular fitness × gender (girl), <i>i3</i>	- ^b						0.20	0.09	0.032			
Motor skills → Cognitive function → Math performance												
<i>Cognitive function</i>												
Motor skills, <i>a</i>	0.15	0.06	0.011	0.16	0.07	0.020	0.29	0.06	<0.001**	0.12	0.06	0.025
<i>Arithmetic skills</i>												
Cognitive function, <i>b1</i>	0.29	0.06	<0.001**	0.20	0.06	<0.001**	0.30	0.06	<0.001**	0.48	0.05	<0.001**
Motor skills, <i>c1</i>	0.14	0.07	0.042	0.15	0.07	0.031	- ^c			0.12	0.07	0.067
<i>Teacher-rated math</i>												
Cognitive function, <i>b2</i>	0.15	0.06	0.016	0.16	0.06	0.010	0.33	0.06	<0.001**	0.45	0.05	<0.001**
Motor skills, <i>c2</i>	0.22	0.07	0.002*	0.21	0.07	0.002*	- ^c			0.18	0.06	0.004*

* $p < 0.01$, ** $p < 0.001$.

Note. All the models were adjusted for age, sex, pubertal stage, body fat percentage, mother's education and learning difficulties.

The *a*, *b1*, *b2*, *c1*, *c2*, *i1*, *i2* and *i3* are the paths in the model (see Figure 1).

^a There were no significant association between physical activity/fitness and cognitive function based on the correlations/ linear regression models and therefore, no path modeling was conducted. ^b Based on the linear regression models, there was no significant interaction between physical activity/fitness and gender. ^c A mediator model fitted the data adequate well without direct effect of physical activity/fitness/motor skills on math performance.

Abbreviations: B = standardized regression coefficient; PA = physical activity; PAL= Paired Associates Learning; RVP, Rapid Visual Information Processing; SE = standard error; SWM = Spatial Working Memory.

Table 3. The estimation results of the mediator models of physical activity/fitness/motor skills on math performance through a paper and pen measured cognitive function test.

	Similarities			Matrix reasoning			Coding			Spatial relations		
	<i>B</i>	<i>SE</i>	<i>p</i>	<i>B</i>	<i>SE</i>	<i>p</i>	<i>B</i>	<i>SE</i>	<i>p</i>	<i>B</i>	<i>SE</i>	<i>p</i>
Self-reported PA → Cognitive function test → Math performance												
<i>Cognitive function test</i>	-									-		
Self-reported PA, <i>a</i>				0.19	0.09	0.034	0.17	0.08	0.049			
Self-reported PA × gender (girl), <i>i1</i>				-0.24	0.18	0.199	-0.17	0.18	0.350			
<i>Arithmetic skills</i>	-									-		
Cognitive function test, <i>b1</i>				0.38	0.05	<0.001**	0.32	0.05	<0.001**			
<i>Teacher-rated math</i>	-									-		
Cognitive function, <i>b2</i>				0.48	0.04	<0.001**	0.28	0.05	<0.001**			
Aerobic fitness → Cognitive function test → Math performance												
<i>Cognitive function test</i>				-			-			-		
Aerobic fitness, <i>a</i>	-0.21	0.10	0.034									
Aerobic fitness × gender (girl), <i>i1</i>	0.25	0.09	0.005*									
<i>Arithmetic skills</i>				-			-			-		
Cognitive function test, <i>b1</i>	0.31	0.06	<0.001**									
Aerobic fitness, <i>c1</i>	0.10	0.09	0.286									
Aerobic fitness × gender (girl), <i>i2</i>	0.15	0.09	0.081									
<i>Teacher-rated math</i>				-			-			-		
Cognitive function test, <i>b2</i>	0.32	0.06	<0.001**									
Aerobic fitness, <i>c2</i>	0.20	0.10	0.045									
Aerobic fitness × gender (girl), <i>i3</i>	0.09	0.10	0.335									
Muscular fitness → Cognitive function → Math performance												
<i>Cognitive function test</i>	-			-			-					
Muscular fitness, <i>a</i>										-0.14	0.10	0.148
Muscular fitness × gender (girl), <i>i1</i>										0.22	0.10	0.027
<i>Arithmetic skills</i>	-			-			-					
Cognitive function test, <i>b1</i>										0.35	0.06	<0.001**
Muscular fitness, <i>c1</i>										0.00	0.09	0.993
Muscular fitness × gender (girl), <i>i2</i>										0.15	0.09	0.097
<i>Teacher-rated math</i>	-			-			-					
Cognitive function test, <i>b2</i>										0.37	0.06	<0.001**
Muscular fitness, <i>c2</i>										0.12	0.09	0.171
Muscular fitness × gender (girl), <i>i3</i>										0.17	0.09	0.050
Motor skills → Cognitive function test → Math performance												
<i>Cognitive function test</i>							-					
Motor skills, <i>a</i>	-0.24	0.09	0.011	0.14	0.06	0.031				0.15	0.07	0.025
Motor skills × gender (girl), <i>i1</i>	0.21	0.09	0.024									
<i>Arithmetic skills</i>							-					

Cognitive function test, <i>b1</i>	0.34	0.06	<0.001**	0.36	0.06	<0.001**		0.35	0.06	<0.001**
Motor skills, <i>c1</i>	0.20	0.06	0.002*	0.13	0.07	0.055		0.13	0.06	0.022
<i>Teacher-rated math</i>										
Cognitive function test, <i>b2</i>	0.35	0.06	<0.001**	0.45	0.04	<0.001**	-	0.37	0.05	<0.001**
Motor skills, <i>c2</i>	0.26	0.06	<0.001**	0.17	0.06	0.004*		0.18	0.08	0.021

* $p < 0.01$, ** $p < 0.001$.

Note. All the models were adjusted for age, sex, pubertal stage, body fat percentage, mother's education and learning difficulties. The *a*, *b1*, *b2*, *c1*, *c2*, *i1*, *i2* and *i3* are the paths in the model (see Figure 1).

Abbreviations: B = standardized regression coefficient; PA = physical activity; PAL= Paired Associates Learning; RVP, Rapid Visual Information Processing; SE = standard error; SWM = Spatial Working Memory.

Table 4. The indirect associations of physical activity/fitness/motor skills on math performance through a computer-assisted cognitive function test.

	Mediator variables											
	Flanker			PAL			SWM			RVP		
	<i>b</i>	<i>SE</i>	<i>p</i>	<i>b</i>	<i>SE</i>	<i>p</i>	<i>b</i>	<i>SE</i>	<i>p</i>	<i>b</i>	<i>SE</i>	<i>p</i>
BOYS †												
<i>Self-reported physical activity</i>	-.‡			-.‡								
Arithmetic skills							0.10	0.04	0.016	0.23	0.10	0.021
Teacher-rated math							0.04	0.01	0.014	0.07	0.03	0.022
<i>Muscular fitness</i>												
Arithmetic skills	0.07	0.04	0.072				0.02	0.06	0.726	0.14	0.07	0.047
Teacher-rated math	0.01	0.01	0.113				0.01	0.02	0.725	0.04	0.02	0.043
<i>Motor skills</i>												
Arithmetic skills	0.09	0.04	0.023	0.07	0.03	0.046	0.19	0.06	<0.001**	0.13	0.06	0.023
Teacher-rated math	0.02	0.01	0.068	0.02	0.01	0.070	0.07	0.02	0.001*	0.04	0.02	0.023
GIRLS †												
<i>Self-reported physical activity</i>	-.‡			-.‡								
Arithmetic skills							0.10	0.04	0.016	-0.02	0.06	0.710
Teacher-rated math							0.04	0.01	0.014	-0.01	0.02	0.709
<i>Muscular fitness</i>												
Arithmetic skills	0.07	0.04	0.072				0.17	0.06	0.003*	0.14	0.07	0.047
Teacher-rated math	0.01	0.01	0.113				0.06	0.02	0.003*	0.04	0.02	0.043
<i>Motor skills</i>												
Arithmetic skills	0.09	0.04	0.023	0.07	0.03	0.046	0.19	0.06	<0.001**	0.13	0.06	0.023

* $p < 0.01$, ** $p < 0.001$.

Note. All the models were adjusted for age, sex, pubertal stage, body fat percentage, mother's education and learning difficulties.

† The indirect effects were estimated as equal in the boys and girls whenever interaction terms were not needed.

‡ There were no significant association between physical activity/fitness and cognitive function based on the correlations/ linear regression models and therefore, no path modeling was conducted.

Abbreviations: b = unstandardized indirect effect; PAL = Paired Associates Learning; RVP = Rapid Visual Information Processing; SE = standard error; SWM = Spatial Working Memory

Table 5. The indirect associations of physical activity/fitness/motor skills on math performance through a pen and paper measured cognitive function test.

	Mediator variables											
	Similarities			Matrix reasoning			Coding			Spatial relations		
	<i>b</i>	<i>SE</i>	<i>p</i>	<i>b</i>	<i>SE</i>	<i>p</i>	<i>b</i>	<i>SE</i>	<i>p</i>	<i>b</i>	<i>SE</i>	<i>p</i>
BOYS †												
<i>Self-reported physical activity</i>	-.‡									-.‡		
Arithmetic skills				0.13	0.06	0.036	0.1	0.06	0.058			
Teacher-rated math				0.06	0.03	0.043	0.03	0.02	0.066			
<i>Aerobic fitness</i>				-.‡			-.‡			-.‡		
Arithmetic skills	-0.23	0.12	0.052									
Teacher-rated math	-0.08	0.04	0.047									
<i>Muscular fitness</i>	-.‡			-.‡			-.‡					
Arithmetic skills										-0.11	0.08	0.161
Teacher-rated math										-0.04	0.03	0.158
<i>Motor skills</i>							-.‡					
Arithmetic skills	-0.17	0.07	0.020	0.11	0.05	0.042				0.12	0.06	0.056
Teacher-rated math	-0.06	0.02	0.017	0.04	0.02	0.038				0.04	0.02	0.030
GIRLS †												
<i>Self-reported physical activity</i>	-.‡									-.‡		
Arithmetic skills				0.03	0.06	0.591	0.04	0.05	0.457			
Teacher-rated math				0.01	0.02	0.595	0.01	0.01	0.464			
<i>Aerobic fitness</i>				-.‡			-.‡			-.‡		
Arithmetic skills	0.14	0.09	0.117									

Teacher-rated math	0.05	0.03	0.126						
<i>Muscular fitness</i>	- ‡			- ‡					
Arithmetic skills								0.11	0.07
Teacher-rated math								0.04	0.02
<i>Motor skills</i>								- ‡	
Arithmetic skills	0.03	0.06	0.616	0.11	0.05	0.042			
Teacher-rated math	0.01	0.02	0.617	0.04	0.02	0.038			

* $p < 0.01$, ** $p < 0.001$

Note. All the models were adjusted for age, sex, pubertal stage, body fat percentage, mother's education and learning difficulties.

† The indirect effects were estimated as equal in the boys and girls whenever interaction terms were not needed.

‡ There were no significant association between physical activity/fitness and cognitive function based on the correlations/ linear regression models and therefore, no path modeling was conducted.

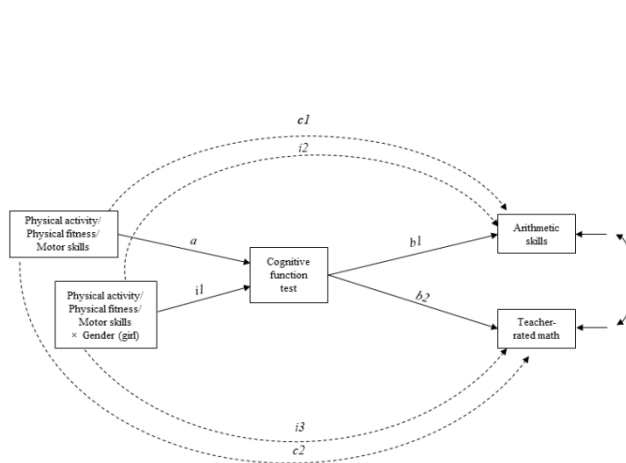
Abbreviations: b = unstandardized indirect effect; PAL = Paired Associates Learning; RVP = Rapid Visual Information Processing; SE = standard error; SWM = Spatial Working Memory

FIGURE LEGENDS

Figure 1. The path diagram of the mediator model linking physical activity/ physical fitness/ motor skills and math performance via cognitive outcomes. Dashed lines denote the associations which were estimated only when needed.

SUPPORTING INFORMATION

Supporting information is available.



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