Longitudinal Associations of Fitness, Motor Competence, and Adiposity with Cognition

Haapala, Eero A

Ovid Technologies (Wolters Kluwer Health)
Longitudinal Associations of Fitness, Motor Competence, and Adiposity with Cognition

Eero A. Haapala¹,², Niina Lintu², Juuso Väistö², Tuomo Tompuri³, Sonja Soininen²,⁴, Anna Viitasalo²,⁵, Aino-Maija Eloranta², Taisa Venäläinen⁶, Arja Sääkslahti¹, Tomi Laitinen³,⁷, and Timo A. Lakka²,⁷,⁸

¹Faculty of Sport and Health Sciences, University of Jyväskylä, Jyväskylä, Finland; ²Institute of Biomedicine, School of Medicine, University of Eastern Finland, Kuopio, Finland; ³Department of Clinical Physiology and Nuclear Medicine, Kuopio University Hospital, Kuopio, Finland; ⁴Social and Health Center, City of Varkaus, Finland; ⁵Novo Nordisk Foundation Center for Basic Metabolic Research, Section of Metabolic Genetics, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark; ⁶Institute of Public Health and Clinical Nutrition, School of Medicine, University of Eastern Finland, Kuopio, Finland; ⁷Institute of Clinical Medicine, University of Eastern Finland, Kuopio Campus, Finland, and ⁸Foundation for Research in Health Exercise and Nutrition, Kuopio Research Institute of Exercise Medicine, Kuopio, Finland

Accepted for Publication: 22 October 2018
Longitudinal Associations of Fitness, Motor Competence, and Adiposity with Cognition

Eero A. Haapala\textsuperscript{1,2}, Niina Lintu\textsuperscript{2}, Juuso Väistö\textsuperscript{2}, Tuomo Tompuri\textsuperscript{3}, Sonja Soininen\textsuperscript{2,4}, Anna Viitasalo\textsuperscript{2,5}, Aino-Maija Eloranta\textsuperscript{2}, Taisa Venäläinen\textsuperscript{6}

Arja Sääkslahti\textsuperscript{1}, Tomi Laitinen\textsuperscript{3,7}, and Timo A. Lakka\textsuperscript{2,7,8}

\textsuperscript{1}Faculty of Sport and Health Sciences, University of Jyväskylä, Jyväskylä, Finland; \textsuperscript{2}Institute of Biomedicine, School of Medicine, University of Eastern Finland, Kuopio, Finland; \textsuperscript{3}Department of Clinical Physiology and Nuclear Medicine, Kuopio University Hospital, Kuopio, Finland; \textsuperscript{4}Social and Health Center, City of Varkaus, Finland; \textsuperscript{5}Novo Nordisk Foundation Center for Basic Metabolic Research, Section of Metabolic Genetics, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark; \textsuperscript{6}Institute of Public Health and Clinical Nutrition, School of Medicine, University of Eastern Finland, Kuopio, Finland; \textsuperscript{7}Institute of Clinical Medicine, University of Eastern Finland, Kuopio Campus, Finland, and \textsuperscript{8}Foundation for Research in Health Exercise and Nutrition, Kuopio Research Institute of Exercise Medicine, Kuopio, Finland

Address correspondence to: Eero A. Haapala, PhD, Sports and Exercise Medicine, Faculty of Sport and Health Sciences, University of Jyväskylä, PO Box 35, FI-40014 University of Jyväskylä, room VIV 247, email: eero.a.haapala@jyu.fi; telephone: +358408054210
The PANIC Study has financially been supported by Ministry of Education and Culture of Finland, Research Committee of the Kuopio University Hospital Catchment Area (State Research Funding), Finnish Innovation Fund Sitra, Social Insurance Institution of Finland, Finnish Cultural Foundation, Foundation for Paediatric Research, Diabetes Research Foundation in Finland, Finnish Foundation for Cardiovascular Research, Juho Vainio Foundation, Paavo Nurmi Foundation, Yrjö Jahnsson Foundation, and the city of Kuopio. Moreover, the PhD students and postdoctoral researchers of the PANIC Study have been supported by Program for Clinical Research and Program for Health Sciences of Doctoral School of University of Eastern Finland, Finnish Doctoral Programs in Public Health, Päivikki and Sakari Sohlberg Foundation, Paulo Foundation, Jalmari and Rauha Ahokas Foundation, Aarne and Aili Turunen Foundation, Finnish Medical Foundation, Jenny and Antti Wihuri Foundation, Kuopio Naturalists' Society, Olvi Foundation, the Aino Eenola and Orion Trusts of Finnish Medical Foundation, the Foundation for Diabetes Research, and the city of Kuopio. The work of Dr. Haapala was part of the University of Jyväskylä profiling area of multidisciplinary brain research funded by Academy of Finland. The sponsors had no role in designing the study, the collection, analysis, or interpretation of the data, the writing of the report, or the decision to submit the manuscript for publication. The authors declare that there are no conflicts of interest.

The results of the present study do not constitute endorsement by ACSM. The Authors declare that the results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.
ABSTRACT

Purpose: To investigate the longitudinal associations of cardiorespiratory fitness (CRF), motor competence (MC), and body fat percentage (BF%) with cognition in children.

Methods: Altogether 371 children (188 boys, 183 girls) aged 6–9 years at baseline participated in this 2-year follow-up study. We assessed CRF by maximal cycle ergometer test, computed the MC score from the z-scores of 50-metre shuttle run, static balance, and box and block test results, measured BF% by dual-energy X-ray absorptiometry, and assessed cognition using the Raven’s Coloured Progressive Matrices (RCPM) score. The associations were studied by linear regression analysis and analysis of covariance with repeated measures.

Results: In boys, a higher MC score (β=-0.161, 95% CI=-0.314 to -0.009), a shorter 50-metre shuttle run test duration (β=0.152, 95% CI=0.007 to 0.296), and a higher number of cubes moved in the BBT (β=-0.161, 95% CI=-0.309 to -0.013) at baseline were associated with a smaller increase in the RCPM score during follow-up. These associations were largely explained by the RCPM score at baseline. However, boys in the highest third (mean difference=2.5, 95% CI for difference=0.66 to 4.33) and the middle third (mean difference=2.1, 95% CI for difference=0.39 to 3.82) of the MC score at baseline had a higher RCPM score over the 2-year follow-up than boys in the lowest third. CRF, MC, or adiposity were not associated with the RCPM score in girls. Changes in CRF, MC, or BF% were not associated with changes in cognition.

Conclusions: Higher MC at baseline predicted better cognition during the first two school years in boys but not in girls. CRF or adiposity was not associated with cognition in boys or girls.

Key words: Cardiorespiratory fitness, motor skills, cognitive functions, obesity, children, youth
INTRODUCTION

Evidence on the positive associations of cardiorespiratory fitness (CRF) and motor competence (MC), and the negative associations of overweight and obesity with cognition and academic achievement in children is emerging (1,2). However, the evidence is mainly based on the results of cross-sectional studies that suggest fairly consistent positive associations of CRF and MC and negative associations of overweight and obesity with cognition and academic achievement in children and adolescents (1–3).

Some studies have demonstrated positive associations of CRF and MC at baseline with cognition (4,5) and academic performance (6,7) after 1–2 years of follow-up in children and adolescents. In longitudinal studies, children and adolescents with continuously higher levels of CRF have been found to have better cognition and academic performance than other children and adolescents over 2-year follow-up (8,9). Although the results of some longitudinal studies suggest that larger improvement in CRF is associated with greater improvement in academic performance (10), other studies have found only weak associations of changes in CRF with changes in cognition or academic performance in youth (8,9).

Overweight, obesity, and increased body fat percentage (BF%) measured by dual-energy x-ray absorptiometry (DXA) or magnetic resonance imaging (MRI) have been associated with decreased brain volumes and impaired cognition and academic achievement among children and adolescents in cross-sectional studies (11–13). Moreover, the results of some longitudinal studies (14,15), but not all of them (16,17), suggest that increased BF% and body mass index (BMI) are associated with impaired cognitive performance in school-aged children. On the contrary, Bisset
et al. (16) reported that underweight, but not overweight, was associated with impaired academic performance in children.

Evidence on the longitudinal associations of CRF, MC, and adiposity with cognition in children is sparse. Furthermore, few studies in population samples of children have utilised specific measures of CRF, MC, and adiposity in relation to cognition. We therefore investigated the associations of CRF assessed by maximal workload during a cycle ergometer exercise test, MC assessed by standardised motor ability tests, and BF% measured by DXA at baseline with the Raven’s Coloured Progressive Matrices (RCPM) score at 2-year follow-up and with changes in the RCPM score during 2-year follow-up in a population sample of children aged 6–9 years at baseline. We also studied the associations of changes in CRF, MC, and BF% with changes in the RCPM over 2-year follow-up.

METHODS

Study design and study population
The present data are from the Physical Activity and Nutrition in Children (PANIC) Study, which is an ongoing follow-up and physical activity and dietary intervention study in a population sample of children from the city of Kuopio, Finland. Altogether 736 children 6–9 years of age from primary schools of Kuopio were invited to participate in the baseline examination in 2007–2009. Altogether 512 children (70% of those invited) participated in the baseline examinations and were divided in the intervention group (306 children) and the control group (200 children). We excluded six children from the study at baseline because of physical disabilities that could hamper participation in the intervention or no time or motivation to attend in the study. The participants did not differ in sex distribution, age, or BMI standard deviation score (BMI-SDS)
from all children who started the first grade in 2007–2009 based on data from the standard school health examinations performed for all Finnish children before the first grade (data not shown). Altogether 440 (87%) of all 506 children included in the intervention study also attended in the 2-year follow-up examinations. Complete data on variables used in the analyses on the associations of CRF, MC, and BF% at baseline with cognition at 2-year follow-up were available for 371 children (188 boys, 183 girls). Complete data on variables used in the analyses on the associations of changes in CRF, MC, and BF% with changes in cognition during 2-year follow-up were available for 299 children (151 boys, 148 girls). Children who had complete baseline data for the analyses were faster in 50-metre shuttle run test than those who did not (p=0.015). There were no differences in other characteristics between children with complete data and those without it. The study protocol was approved by the Research Ethics Committee of the Hospital District of Northern Savo. Both children and their parents gave their written informed consent.

Assessment of body size and composition
Body weight was measured twice the children after having fasted for 12 hours, having emptied the bladder, and standing in light underwear by a calibrated InBody® 720 bioelectrical impedance device (Biospace, Seoul, South Korea) to accuracy of 0.1 kg. The mean of these two values was used in the analyses. Body height was measured three times the children standing in the Frankfurt plane without shoes using a wall-mounted stadiometer to accuracy of 0.1 cm. The mean of the nearest two values was used in the analyses. BMI was calculated by dividing body weight (kg) by body height (m) squared. BMI- SDS was calculated based on the Finnish references (18). The prevalence of overweight and obesity was defined using the cut-off values provided by Cole et al. (19). Total fat mass, BF%, and lean body mass (LM) were measured by
the Lunar® dual-energy X-ray absorptiometry device (GE Medical Systems, Madison, WI, USA) using standardised protocols.

**Assessment of cardiorespiratory fitness and motor competence**

CRF was assessed using a maximal exercise test with an electromagnetically braked Ergoselect 200K® cycle ergometer (Ergoline, Bitz, Germany) (20). The exercise test protocol included a 3-minute warm-up period at 5 Watts (W), a 1-minute steady-state period at 20 W, an exercise period with a workload increase of 1 W every 6 seconds until exhaustion and a 4-minute cooling-down period at 5 W. The exercise test was considered maximal if the reason for terminating the test indicated maximal effort and maximal cardiopulmonary capacity. CRF was defined as maximal workload at the end of the exercise test per kilogram of LM.

Speed and agility were assessed by the 50-metre shuttle run test (21). The children were asked to run five metres from a starting line to another line as fast as possible, to turn on the line, to run back to the starting line, and to continue until five shuttles were completed. The test score was the running time in seconds, with a longer time indicating a poorer performance.

Static balance was assessed by the modified flamingo balance test (22). The children were asked to stand barefoot on one self-chosen leg with eyes closed for 30 seconds. The test score was the number of floor touches with a free foot or eye openings during 30 seconds, a higher number of floor touches and eye openings indicating poorer static balance.

Manual dexterity and upper limb movement speed were assessed by the box and block test (23). The children were asked to pick up small wooden cubes (2.5 cm per side) one by one with the dominant hand from one side of a wooden box (53.7 cm × 25.4 cm × 8 cm) and to move as many cubes as possible to the other side of the box during 60 seconds and to repeat the same task with
the nondominant hand. The test score was the total number of cubes moved to the other side of the box during 120 seconds, a smaller number of cubes moved indicating poorer manual dexterity.

We computed the MC score as the sum of sex-specific z-scores for the test scores of the 50-metre shuttle run test (inverse), the modified flamingo balance test (inverse), and the box and block test as described previously (6,22). A higher score indicates better MC.

Assessment of cognition
Nonverbal reasoning was assessed using the Raven Coloured Progressive Matrices (RCPM) (24) that was administered by trained researchers at the Institute of Biomedicine, University of Eastern Finland. The RCPM has been suggested to represent higher-order executive functioning that involves all core components of it: inhibition, working memory, and mental flexibility (25). The RCPM requires the ability to find similarities, differences, and discrete patterns and does not depend on acquired knowledge or language skills (24). The RCPM includes three sets of 12 items. Each test page includes a large item or a pattern of items and six small items. The child was asked to select the correct small item, which completes the large item or the set of items. The RCPM score was the number of correct answers, ranging from zero to 36.

Other assessments
The parents were asked to report in a questionnaire their annual household income, (≤30,000 €, 30,001–60,000 €, ≥ 60,001 €) and their highest completed or ongoing educational degrees (vocational school or less, polytechnic, university). The degree of the more educated parent was used in the analyses. The research physician assessed pubertal status using the 5-stage scale described by Tanner (26). The boys were defined as having entered clinical puberty if their
testicular volume assessed by an orchidometer was \( \geq 4 \) mL (stage \( \geq 2 \)). The girls were defined having entered clinical puberty if their breast development had started (stage \( \geq 2 \)). Maturity offset as a measure of age from peak height velocity was computed using a sex-specific formula described by Moore et al. (27).

Statistical methods
We performed all statistical analyses using the SPSS Statistics, Version 23.0 (IBM Corp., Armonk, NY, USA). All statistical analyses were run separately for boys and girls because we observed that sex partly modified the associations between MC at baseline and the RCPM score at baseline (\( p = 0.004 \) for interaction) and 2-year follow-up (\( p = 0.082 \) for interaction) and the association between CRF at baseline and the RCPM at 2-year follow-up (\( p = 0.077 \) for interaction). Basic characteristics between boys and girls were compared using the Student’s t-test for normally distributed continuous variables, the Mann–Whitney U test for skewed continuous variables, and the Chi-square test for dichotomous variables. We analysed the associations of CRF, the measures of MC, and BF% at baseline with the RCPM score at 2-year follow-up using linear regression analyses adjusted for age and the study group. These observational data were adjusted for the study group because the PANIC study is originally a controlled physical activity and dietary intervention study (28). Although we did not observe a statistically significant effect of the intervention on the RCPM score, the current data were adjusted for the study group to account of the residual confounding. These data were additionally adjusted for the RCPM score at baseline. The associations of changes in CRF, MC, and BF% with changes in the RCPM score were analysed using linear regression analyses adjusted for age and the study group. These data were further adjusted for the RCPM score and either CRF, MC, or BF% at baseline. Differences in the RCPM score over 2-year follow-up between the thirds of
CRF, MC, and BF% were investigated using analyses of covariance with repeated measures adjusted for age and the study group. After age and study group adjustments all data were additionally adjusted for pubertal status, maturity offset, parental education, or household income at baseline, which were entered one by one into the model.

RESULTS

Basic characteristics at baseline
Boys were taller and heavier and had lower maturity offset and BF% than girls (Table 1). Boys also had higher CRF and a shorter 50-metre shuttle run test duration and moved less cubes in two minutes in the box and block test compared to girls.

Associations of CRF, MC, and BF% at baseline with RCPM score at 2-year follow-up
In boys, higher CRF at baseline was associated with a lower RCPM score at 2-year follow-up after adjustment for age and the study group (Table 2). The inverse association between CRF at baseline and RCPM score at 2-year follow-up in boys was no longer statistically significant after further adjustment for the RCPM score at baseline (β = -0.100, 95% CI = -0.222 to 0.022, p = 0.108). Moreover, the associations of the MC score (β = -0.002, 95% CI = -0.131 to 0.127, p = 0.972), time spent in the 50-metre shuttle run test (β = 0.019, 95% CI = -0.103 to 0.141, p = 0.760), the number of cubes moved in the box and block test (β = -0.045, 95% CI = -0.169 to 0.079, p = 0.478), errors in the flamingo balance test (β = -0.057, 95% CI = -0.178 to 0.064, p = 0.352), and BF% (β = 0.058, 95% CI = -0.059 to 0.176, p = 0.328) with the RCPM score were further attenuated after adjustment for the RCPM score at baseline. Adjustment for pubertal
status, maturity offset, parental education, or household income had no effect on these associations.

In girls, CRF, the MC score, time spent in the 50-metre shuttle run test, the number of cubes moved in the box and block test, errors in the flamingo balance test, or BF% at baseline was not associated with the RCPM score at 2-year follow-up (Table 2). Further adjustment for the RCPM score, pubertal status, maturity offset, parental education, or household income at baseline had no effect on these associations.

**Associations of CRF, MC, and BF% at baseline with changes in RCPM score during 2-year follow-up**

In boys, a higher MC score (β = -0.161, 95% CI = -0.314 to -0.009, p = 0.039), a shorter 50-metre shuttle run test duration (β = 0.152, 95% CI = 0.007 to 0.296, p = 0.040), and a larger number of cubes moved in the box and block test (β = -0.161, 95% CI = -0.309 to -0.013, p = 0.033) at baseline were associated with a smaller increase in the RCPM score during 2-year follow-up after adjustment for age and the study group. None of these associations remained statistically significant after further adjustment for the RCPM score at baseline (data not shown).

In girls, CRF, the MC score, 50-metre shuttle run test duration, the number of cubes moved in the box and block test, or BF% at baseline was not associated with the change in RCPM score during 2-year follow-up.

**Associations of changes in CRF, MC, and BF% with changes in RCPM score during 2-year follow-up**

Changes in CRF, the MC score, 50-metre shuttle run test duration, the number of cubes moved in the box and block test, errors in the flamingo balance test, and BF% were not associated with
changes in the RCPM score in boys or girls after adjustment for age and the study group. These associations remained similar after further adjustment for the RCPM score and the corresponding measure of CRF, MC, and BF% at baseline.

**Differences in RCPM score over 2-year follow-up in thirds of CRF, MC, and BF% at baseline**

Boys in the highest third (mean difference 2.5, 95% CI for mean difference = 0.66 to 4.33, p = 0.004) and the middle third (mean difference 2.1, 95% CI for mean difference = 0.39 to 3.82, p = 0.010) of the MC score at baseline had a higher RCPM score than boys in the lowest third over the 2-year follow-up after adjustment for age and the study group (Figure 1). There were no differences in the RCPM score among the thirds of CRF, 50-metre shuttle run test duration, the number of cubes moved in the box and block test, errors in the flamingo balance test, or BF% in boys. Further adjustment for pubertal status, maturity offset, parental education, or household income at baseline had no effect on these differences.

There were no differences in the RCPM score among the thirds of CRF, the MC score, 50-metre shuttle run test duration, the number of cubes moved in the box and block test, errors in the balance test, or BF% in girls.

**Associations of RCPM score at baseline with RCPM score at 2-year follow-up and changes in RCPM score, CRF, MC, and adiposity during 2-year follow-up**

The RCPM score at baseline was positively related to the RCPM score at 2-year follow-up in boys ($\beta = 0.601$, 95% CI = 0.482 to 0.720, $p < 0.001$) and girls ($\beta = 0.552$, 95% CI = 0.426 to 0.679, $p < 0.001$). The RCPM score at baseline was inversely associated with the change in the RCPM score during 2-year follow-up in boys ($\beta = -0.720$, 95% CI = -0.832 to -0.608, $p < 0.001$)
and girls ($\beta = -0.714$, 95% CI = -0.848 to -0.634, $p < 0.001$). In boys, a higher RCPM score at baseline was also related to a smaller decrease in 50-metre shuttle run test duration after adjustment for age and the study group ($\beta = -0.165$, 95% CI = -0.329 to 0.000, $p = 0.049$). Further adjustment for pubertal status, maturity offset, parental education, or household income had no effect on these associations.

**DISCUSSION**

We found that a lower MC score at baseline was associated with poorer cognition at 2-year follow-up in boys and that boys in the lowest third of the MC score at baseline had poorer cognition over 2-year follow-up than boys in other thirds. However, CRF or adiposity was not associated with cognition in boys and CRF, MC, or adiposity was not related to cognition in girls. We also observed that cognitive performance at baseline was a strong predictor of cognition two years later in boys and girls and that cognition at baseline partly explained the longitudinal associations of CRF, MC, and adiposity with cognition in boys.

Our findings along with the limited evidence from previous longitudinal studies (8,9,29) suggest that changes in CRF and MC have weak and inconsistent associations with changes in cognition and academic achievement in children. One study among children aged 11–14 years at baseline (30) reported that improvement in 20-metre endurance shuttle run test performance during 3-year follow-up period was related to better academic achievement at follow-up. However, these data were not adjusted for academic achievement at baseline and therefore it is not known whether improved CRF was associated with improved academic achievement. We observed a positive association of MC at baseline with the RCPM score at 2-year follow-up but a negative
association with changes in the RCPM score over 2-year follow-up. However, these association were explained by the RCPM score at baseline. These results suggest that cognition and academic performance at baseline may be stronger determinants of subsequent cognitive and academic performance than changes in CRF and MC among children.

We observed that boys in the lowest third of the MC score at baseline had consistently poorer cognition over 2-year follow-up. We have previously reported that children with lower MC at baseline had poorer reading and arithmetic skills in Grades 1–3 (6). Furthermore, children with lower CRF and poorer cognitive performance at baseline have been found to exhibit larger gains in cognitive performance over 1-year follow-up than children with higher CRF and better cognitive performance at baseline (4). These partly contrasting findings between cross-sectional and longitudinal studies maybe related to the regression towards the mean phenomenon during growth and maturation. This means that boys with poorer cognitive performance at baseline may have reached other boys at 2-year follow-up by change or because of improvement in cognitive ability related to normal growth and maturation.

It is also possible that the development of MC and cognitive skills may have a more interwoven relationship in early childhood than in middle and late childhood or in adolescence (3,31). Therefore, early developing children may have better MC and cognitive skills than late developing children that results in cross-sectional differences in cognition between children with different levels of MC (3,22). This hypothesis is partly supported by our findings that a higher RCPM score at baseline was associated with a smaller change in RCPM score and smaller improvement in 50-metre shuttle run test duration among boys during 2-year follow-up. We have previously reported that boys with a lower RCPM score at baseline also had a poorer 50-metre shuttle run test performance at baseline than other boys (22) and in the present study, we showed
that these boys improved their RCPM score and 50-metre shuttle run test performance more than other boys over 2-year follow-up. These results suggest that differences in cognition related to MC in cross-sectional studies may reflect differences in the rate and stage of neuromuscular and cognitive development. Another explanation for these observations may be that opportunities for MC enhancing physical activity during early childhood may also improve cognition (31).

We found that adiposity was not associated with cognition in children. This is in contrast to previous findings demonstrating a negative association of BF% measured either by DXA or MRI with cognition in children (12,14,32). Although impaired cognition has been linked to larger gains in adiposity among children and adults suggesting a bidirectional association between adiposity and cognition (33), we found no association of cognition at baseline with change in BF% during the 2-year follow-up. One reason for these contrasting observations may be that the aspects of cognition used in previous studies, such as inhibition, working memory, and executive functions, may be more sensitive to changes in adiposity and vice versa than the RCPM score.

We found a weak if any association of CRF, MC, or adiposity with cognition in girls. This observation is in line with the results of previous studies suggesting that CRF and MC are more strongly related to cognition and academic achievement in boys than in girls (6,22,34). The reason for these findings is not known, but it may relate to a more rapid maturation process in girls than in boys. Furthermore, there is some evidence that the size of the brain areas linked to CRF, MC, and cognition, such as basal ganglia, peaks earlier in girls than in boys (35,36). Therefore, it is possible that the magnitude of the associations of CRF, MC, and adiposity with cognition is different in girls and boys and among age and developmental groups (3).

In contrast to the positive association between CRF and cognition observed in most previous cross-sectional studies (1,29), we found a negative relationship of CRF at baseline with cognition
at 2-year follow-up, although this association was attenuated after controlling for cognition at baseline. Our observations are in line with the results of other studies on weak associations of CRF, assessed by cycle ergometer exercise tests, with cognition and academic achievement among children (6,22,37,38). Most previous studies on the associations of CRF with cognition have utilised either indirect field measures of CRF, such as the 20 metre shuttle run test, or have compared cognitive functions between children with very high and very low maximal oxygen uptake (1,29). Field measures of CRF and maximal oxygen uptake normalised for body mass reflect not only CRF but also adiposity and MC (39). In contrast, a cycle ergometer exercise test is relatively independent of MC (40) and does not require supporting body mass. Furthermore, we normalised CRF for LM that has been recommended to take body size and composition into account in the assessment of CRF (39). Another reason maybe that hippocampal depended memory and inhibition are more sensitive to changes in CRF (1) than non-verbal reasoning. Finally, some longitudinal evidence suggests that childhood cognition is a stronger determinant of adulthood cognition than adulthood CRF, suggesting that the link between cognition and CRF is neuroselective rather than neuroprotective (41).

The strengths of our study include the longitudinal study design, the large population sample of boys and girls and the valid and comprehensive assessments of CRF, MC, adiposity, and cognition. We were also able to control the data for important confounding factors such as pubertal status and socioeconomic positioning. A weakness of the study is that we utilised only one measure of cognition instead of a more comprehensive testing of different components of cognition. Furthermore, this observational study was concentrated on the associations of CRF, MC, and BF% with cognition and therefore these results cannot be used to draw causal conclusions on the effects of physical activity and dietary intervention on cognition.
In conclusion, we observed that boys in the lowest third of MC score at baseline had poorer cognition over 2-year follow-up than those in the middle and highest thirds of MC score at baseline. However, we found no evidence for the associations of changes in CRF, MC, or adiposity with changes in cognition during 2-year follow-up among boys. In girls, CRF, MC, and adiposity exhibited weak if any relationships to cognition. Our results suggest that cross-sectional differences in cognition among boys with different levels of MC persist over 2-year follow-up. More longitudinal studies starting from infancy are warranted to investigate the trajectories of cognitive development related to CRF, MC, and adiposity in children.

ACKNOWLEDGEMENTS
The authors are grateful to all the children and their parents for participating in the PANIC study. The authors are also indebted to the members of the PANIC research team for their skilful contribution in performing the study. The PANIC Study has financially been supported by Ministry of Education and Culture of Finland, Research Committee of the Kuopio University Hospital Catchment Area (State Research Funding), Finnish Innovation Fund Sitra, Social Insurance Institution of Finland, Finnish Cultural Foundation, Foundation for Paediatric Research, Diabetes Research Foundation in Finland, Finnish Foundation for Cardiovascular Research, Juho Vainio Foundation, Paavo Nurmi Foundation, Yrjö Jahnsson Foundation, and the city of Kuopio. Moreover, the PhD students and postdoctoral researchers of the PANIC Study have been supported by Program for Clinical Research and Program for Health Sciences of Doctoral School of University of Eastern Finland, Finnish Doctoral Programs in Public Health, Päivikki and Sakari Sohlberg Foundation, Paulo Foundation, Jalmari and Rauha Ahokas Foundation, Aarne and Aili Turunen Foundation, Finnish Medical Foundation, Jenny and Antti
Wihuri Foundation, Kuopio Naturalists' Society, Olvi Foundation, the Aino Eerola and Orion Trusts of Finnish Medical Foundation, the Foundation for Diabetes Research, and the city of Kuopio. The work of Dr. Haapala was part of the University of Jyväskylä profiling area of multidisciplinary brain research funded by Academy of Finland. The sponsors had no role in designing the study, the collection, analysis, or interpretation of the data, the writing of the report, or the decision to submit the manuscript for publication. The authors declare that there are no conflicts of interest.

The results of the present study do not constitute endorsement by ACSM. The Authors declare that the results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.
REFERENCES


FIGURE CAPTION

Figure 1. Differences in the Raven’s Coloured Progressive Matrices (CPM) score over 2-year follow-up in boys in the thirds of motor competence score at baseline. Data are estimated marginal means and their 95% confidence intervals (CI) from analysis of covariance for repeated measures adjusted for age and study group.
Figure 1

Motor competence

Raven's CPM score

Baseline 2-year follow-up

Lowest third

Middle third

Highest third
Table 1. Basic characteristics at baseline

<table>
<thead>
<tr>
<th></th>
<th>Boys N=188</th>
<th>Girls N=183</th>
<th>P for difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>7.6 (0.3)</td>
<td>7.6 (0.4)</td>
<td>0.240</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>129.6 (5.2)</td>
<td>127.8 (5.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>26.9 (6.1)</td>
<td>25.5 (5.8)*</td>
<td>0.045</td>
</tr>
<tr>
<td>BMI-SDS</td>
<td>-0.18 (1.1)</td>
<td>-0.19 (1.1)</td>
<td>0.960</td>
</tr>
<tr>
<td>Prevalence of overweight and obesity (%)</td>
<td>12.8</td>
<td>14.4</td>
<td>0.654</td>
</tr>
<tr>
<td>Body fat percentage (%)</td>
<td>15.6 (10.9)</td>
<td>20.5 (10.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Puberty at baseline (%)</td>
<td>0.7</td>
<td>4.1</td>
<td>0.054</td>
</tr>
<tr>
<td>Maturity offset at baseline</td>
<td>-4.4 (0.3)</td>
<td>-3.6 (0.3)*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Parental education (%)</td>
<td></td>
<td></td>
<td>0.083</td>
</tr>
<tr>
<td>Vocational school or less</td>
<td>18.8</td>
<td>17.5</td>
<td></td>
</tr>
<tr>
<td>Polytechnic</td>
<td>40.9</td>
<td>51.9</td>
<td></td>
</tr>
<tr>
<td>University degree</td>
<td>40.3</td>
<td>30.6</td>
<td></td>
</tr>
<tr>
<td>Household income (%)</td>
<td></td>
<td></td>
<td>0.341</td>
</tr>
<tr>
<td>0-30 000</td>
<td>16.4</td>
<td>19.3</td>
<td></td>
</tr>
<tr>
<td>30 001-60 000</td>
<td>43.7</td>
<td>48.1</td>
<td></td>
</tr>
<tr>
<td>≥60 001</td>
<td>39.9</td>
<td>32.6</td>
<td></td>
</tr>
<tr>
<td>Cardiorespiratory fitness (W_max / lean mass)</td>
<td>3.8 (0.5)</td>
<td>3.6 (0.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>50m shuttle run test time (s)</td>
<td>23.7 (2.2)</td>
<td>24.2 (2.0)</td>
<td>0.008</td>
</tr>
<tr>
<td>Cubes moved in the box and block test (n)</td>
<td>99.2 (13.0)</td>
<td>104.9 (12.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Errors in the flamingo balance test (n)</td>
<td>4.0 (4.0)*</td>
<td>3.0 (4.0)*</td>
<td>0.001</td>
</tr>
<tr>
<td>Raven Coloured Progressive Matrices score</td>
<td>23.9 (5.3)</td>
<td>24.2 (5.0)</td>
<td>0.584</td>
</tr>
</tbody>
</table>

Data are from the Student t-test or Mann-Whitney U test for continuous variables and chi-square test for categorical variables and are displayed as means (SD), medians (IQR), or percentages (%). P values refer to statistical significance for differences between boys and girls. W_max = maximal workload achieved in the exercise test.
Table 2. Associations of cardiorespiratory fitness, motor competence, and adiposity at baseline with the Raven’s Coloured Progressive Matrices at 2-year follow-up.

<table>
<thead>
<tr>
<th></th>
<th>Boys N = 188</th>
<th></th>
<th></th>
<th>Girls N=183</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>95% CI</td>
<td>p</td>
<td>β</td>
<td>95% CI</td>
<td>p</td>
</tr>
<tr>
<td>Cardiorespiratory fitness (W&lt;sub&gt;max&lt;/sub&gt;/ lean mass)</td>
<td>-</td>
<td>-0.307 to -</td>
<td>0.041</td>
<td>0.027</td>
<td>-0.128 to 0.730</td>
<td>0.183</td>
</tr>
<tr>
<td>Motor competence score&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.157</td>
<td>0.006</td>
<td>0.290</td>
<td>0.027</td>
<td>-0.128 to 0.183</td>
<td>0.142</td>
</tr>
<tr>
<td>50-metre shuttle run test time (s)</td>
<td>-</td>
<td>-0.246 to 0.189</td>
<td>0.000</td>
<td>-0.155 to 0.995</td>
<td>0.156</td>
<td></td>
</tr>
<tr>
<td>Cubes moved in the box and block test (n)</td>
<td>0.062</td>
<td>-0.089 to 0.214</td>
<td>0.418</td>
<td>-0.168 to 0.801</td>
<td>0.019</td>
<td>0.130</td>
</tr>
<tr>
<td>Errors in the Flamingo balance test (n)</td>
<td>-</td>
<td>-0.234 to 0.264</td>
<td>0.060</td>
<td>-0.209 to 0.433</td>
<td>0.060</td>
<td>0.090</td>
</tr>
<tr>
<td>Body fat percentage (%)</td>
<td>0.056</td>
<td>-0.090 to 0.202</td>
<td>0.448</td>
<td>-0.242 to 0.232</td>
<td>0.092</td>
<td>0.059</td>
</tr>
</tbody>
</table>

Data are standardised regression coefficient and their 95% confidence intervals from multivariate linear regression analyses adjusted for age and study group. <sup>1</sup>Computed from z-scores and the formula 50-m shuttle run time (inverse) + errors in the modified flamingo balance test (inverse) + cubes moved in box and block test.