Features of the Metabolic Syndrome Are Associated With Objectively Measured Physical Activity and Fitness in Danish Children

The European Youth Heart Study (EYHS)

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OBJECTIVE — Features of the metabolic syndrome are becoming increasingly evident in children. Decreased physical activity is likely to be an important etiological factor, as shown previously for subjective measures of physical activity in selected groups. The purpose of this study was to examine the relationship between the metabolic syndrome and objectively measured physical activity and whether fitness modified this relationship.

RESEARCH DESIGN AND METHODS — A total of 589 Danish children (310 girls, 279 boys, mean [±SD] age 9.6 ± 0.44 years, mean weight 33.6 ± 6.4 kg, mean height 1.39 ± 0.06 m) were randomly selected. Physical activity was measured with the uni-axial Computer Science & Applications accelerometer (MTI actigraph) worn at the hip for at least 3 days (≥10 h/day) and fitness with a maximal bike test. As outcomes, we measured sitting systolic and diastolic blood pressure, degree of adiposity (sum of four skinfolds), and, finally, insulin, glucose, triglicerides, and HDL cholesterol in fasting blood samples. The outcome variables were statistically normalized and expressed as the number of SDs from the mean. (i.e., *Z* scores). A metabolic syndrome risk score was computed as the mean of these *Z* scores. Multiple linear regression was used to test the association between physical activity and metabolic risk, adjusted primarily for age, sex, sexual maturation, ethnicity, parental smoking, socioeconomic factors, and the Computer Science & Applications unit, as well as for fitness. Robust SEs were computed by clustering on school.

RESULTS — All children were in the nondiabetic range of fasting glucose. Metabolic risk was inversely related to physical activity ($P = 0.008$). The relationship was weakened after adjustment for fitness, but there was a significantly positive interaction between physical activity and fitness.

CONCLUSIONS — Physical activity is inversely associated with metabolic risk, independently of potential confounders. The interaction between physical activity and fitness suggests that the potential beneficial effect of activity may be greatest in children with lower cardiorespiratory fitness.

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Abbreviations: BP, blood pressure; CSA, Computer Science & Applications.

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The metabolic syndrome is characterized by hyperinsulinemia, low glucose tolerance, hyperlipidemia, hypertension, and obesity. Clustering of these metabolic risk factors has been noted in the pediatric population (1–5). In adults, this clustering of metabolic risk factors has been associated with low levels of physical activity, with some evidence suggesting effect modification by cardiorespiratory fitness (6,7). Population studies on these relationships in randomly selected samples of children are sparse, and none of these have utilized objective measures of physical activity such as accelerometry. Questionnaire-based assessment of physical activity, which is the most common subjective method, is imprecise, particularly in children (8–11). An inverse association between accelerometry-derived physical activity and insulin resistance has recently been observed (12) in Danish children. The aim of the present study was to determine whether metabolic risk factor clustering in this population is associated with physical activity following adjustment for potential confounders including fitness. We also tested whether fitness modified the association between activity and metabolic syndrome (7).

RESEARCH DESIGN AND METHODS

— The study was a school-based, cross-sectional study of pre- or early pubertal children, randomly selected by a two-stage sampling strategy. Data were collected in the academic year 1997–1998 in Odense, Denmark, as part of the European Youth Heart Study (EYHS).

Altogether, 711 8- to 10-year-old children, who attended schools in the county of Odense, Denmark, were invited to participate in the study along with their parents.

All eligible schools were stratified ac-

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cording to location (urban, suburban, and rural) and the socioeconomic profile of the uptake area (high, middle, and low). From each stratum, a proportional, two-stage cluster sample of children was selected. The primary clustering units were the schools. The sampling frame for schools was a complete list of public schools in Odense, from which schools were sampled using probability proportional to school size. The secondary units were the children within the schools, and equal numbers of children were sampled randomly from each school.

Twenty-eight of 35 schools were sampled, and 25 agreed to participate. Of the three nonparticipating schools, one was rural, one was urban from a middle-class area, and one was urban from a low-income area. "Interference with the educational process" was given as the reason for not participating. A total of 711 individuals (58% of the total eligible population) were sampled and invited to participate in the study, and 690 children (97%) responded to the invitation. A total of 589 (310 girls and 279 boys) participated in the study together with their parents (83% of the sampled and 48% of the total eligible population).

The study was approved by the local scientific ethics committee (case no. 96/272) and performed in accordance with the Helsinki Declaration. All parents gave written informed consent for their child to participate, and all children gave verbal consent.

Data collection

Physical examination. Height and weight were measured with a stadiometer and a calibrated scale, respectively. Body composition was assessed by the sum of four skinfolds, measured with Harpenden calipers over the triceps, biceps, and subscapular muscles and superior to the anterior superior iliac spine. This measure has been shown to correlate highly with dual-energy X-ray absorptiometry–measured body fat percentage in similarly aged children (13). Measurements were performed on the left side of the body with the child standing. Two measurements were taken in each position. If there was a difference of >2 mm, a third measurement was taken and the mean of the two closest measurements was used. Measurements were made in rotation (one measurement on each site, then repeated). Sexual maturation was assessed according to Tanner (14).

Blood pressure. Blood pressure (BP) was measured in the sitting position with the Dinamap adult/pediatric and neonatal vital signs monitor (Critikon; GE Medical Systems, Milwaukee, WI), using the left arm. Five measurements of the diastolic and systolic BPs were taken within a 10-min interval. The means of the last three measurements of both diastolic and systolic BP were used in the analysis.

Blood samples. All children and their parents received written information, and the children were asked to fast from the evening before the morning of blood sampling. The fasting samples were taken between 8:00 and 8:30 A.M. Samples were stored at −80°C and analyzed for serum insulin, glucose, total cholesterol, HDL cholesterol, and triglyceride. Cholesterol was analyzed using the cholesterol esterase/oxidase enzymatic method, and triglyceride was analyzed using the lipase/glycerol kinase/glycerol phosphate oxidase enzymatic method. HDL was analyzed using the homogeneous polyanion/cholesterol esterase/oxidase enzymatic method. Glucose was analyzed using the hexokinase method. Blood lipids and glucose were measured on an Olympus AU600 autoanalyzer (Olympus Diagnostica, Hamburg, Germany). Insulin was analyzed using an enzyme immunoassay (microtiter plate format; Dako Diagnostics, Ely, U.K.). The coefficients of variation between batches were as follows: insulin, 6.9% (at 110.4 pmol/l) and 5.9% (at 356.2 pmol/l); glucose, 1.2% (at 3.26 and 14.67 mmol/l); triglyceride, 1.0% (at 4.04 mmol/l); and HDL cholesterol, 1.1% (at 1.88 mmol/l).

Metabolic syndrome risk score. The metabolic syndrome is a cluster of insulin resistance, overweight, dyslipidemia, hypertension, and microalbuminuria (15–17). The definition of the syndrome and cutoff points for its various components vary between studies, but none of these definitions apply specifically to children. As our primary objective was to investigate whether the clustering of risk factors was related to habitual physical activity in a population sample of Danish children, we decided to compute a continuous metabolic syndrome risk score (7) from the following six measurements: insulin, glucose, HDL cholesterol, triglycerides, the sum of four skinfolds, and BP (no information was collected on albumin). This score thus only applies to this population but is more suitable for investigating associations and thus etiology within the cohort (18). For each of these variables, a *Z* score was computed as the number of SD units from the sample mean after normalization of the variables, i.e., $Z = ([\text{value} - \text{mean}]/\text{SD})$. The *Z* scores were multiplied by −1 if necessary to indicate higher metabolic risk with increasing value. The *Z* scores of systolic and diastolic BP were averaged and then added to the rest of the *Z* scores. This sum was then divided by six to compile the metabolic syndrome risk score with units of SD. We also computed a nonobesity metabolic risk score, omitting the *Z* score from the sum of skinfolds.

Physical activity. Habitual physical activity was assessed with the Computer Science & Applications (CSA) accelerometer, now also known as the MTI actigraph (Manufacturing Technology, Fort Walton Beach, FL). The CSA is a uni-axial piezo-electric accelerometer with a dynamic range of ±2.13*g* and a frequency-dependent bandwidth filter that can be regarded as a mathematical weighting function (19,20). The CSA samples acceleration at 10 Hz and integrates this over the user-defined epoch. In this study, the epoch was set at 60 s, comprising an integral of 600 measurements for each data point. The CSA was returned by the participant and data downloaded at the day of the child's physical exam. In order to distinguish true zeros from the zeros recorded when the monitor had been taken off, the field data were cleaned; all CSA files were screened for periods of zero activity. Zero activity periods of 10 min or longer were interpreted as "CSA not worn," and these periods were removed from the summation of activity. Given these criteria, the data were included if the child had accumulated >10 h of activity data per day for at least 3 days. Data are expressed as total counts per registered time to yield a measure of average physical activity intensity. The CSA exhibits good intrainstrument reliability in mechanical setups, but interinstrument differences have been reported (20). All analyses are therefore adjusted for CSA unit. Sixty-four CSA units were used in this study.

Physical fitness. Physical fitness was determined by a maximum cycle-ergometer test, as previously described (21). Briefly, the workload was preprogrammed to in-

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crease on a computerized cycle-ergometer (Monark 839 Ergomedic) every third minute until exhaustion. Initial workload and increments were 20 or 25 W, depending on whether the body mass of the child was below or above 30 kg. Heart rate was registered continuously (Polar Vantage NV; Polar Electro Oy, Kempele, Finland). Criteria for exhaustion were a heart rate >185 bpm, failure to maintain a pedaling frequency of at least 30 revolutions per minute (rpm), and a subjective judgment by the observer that the child could no longer keep up, even after vocal encouragement. All children were tested by the same person. The maximal power output (W_{max}) was calculated as the power in the last fully completed workload plus the power increment of the last step multiplied by the time proportion completed of the last step. Physical fitness was expressed as the maximal power output per kilogram body mass (in W/kg). This measure is highly correlated ($r = 0.90$ in boys and $r = 0.95$ in girls) with directly measured $V_{O_{2max}}$ (21).

Other information. The socioeconomic group of the children was assessed with a parental questionnaire. Both the education and income level of each of the parents were coded according to the Danish National Statistical Registry and then recoded into five-level scores, ranging from 1 to 5. A higher number indicates a higher level of education and income. These two scores were then averaged into the socioeconomic group score, which therefore has nine levels. The parent questionnaire also contained questions on ethnicity (1 = Caucasian, and 0 = other) and parental smoking (coded as 1 = one or both parents smoke, and 0 = none of the parents smoke).

Statistics

All variables were checked for normality and normalized if necessary. The optimal transformation was determined by highest probability of failing the test for skewness and kurtosis. We calculated mean values for the entire sample as well as for the subsample with complete data in exposures and outcomes. Dropout analyses were performed on differences between the subsample and the entire sample to estimate generalizability of subsequent findings.

Multiple linear regression analysis was used for assessing the relationship between physical activity and the metabolic syndrome. The relationships were adjusted for age, sex, sexual maturation, ethnicity, socioeconomic status, parental smoking, and CSA unit. Additional adjustment was made for fitness. The regression analyses were clustered on primary sampling unit (i.e., school) to produce robust SEs. Analyses of the nonobesity metabolic risk score were additionally adjusted for the sum of skinfolds as a covariate. To investigate the possibility of effect modification, analyses were repeated, with inclusion of an interaction between physical activity and fitness. The software STATA version 8.2 (College Station, TX) was used for all statistical analyses, and the level of significance was set at $P = 0.05$.

Several variables required numeric transformation to normalize their distributions. These were insulin, diastolic BP, and physical activity, which were normalized by square root; weight, glucose, triglyceride, skinfold thickness, and systolic BP, which were normalized by the reciprocal square root; and age and HDL, which were logarithmically transformed.

RESULTS

Representativeness

Sampling procedures ensured that the sex distribution reflected the distribution of the Odense region. By comparison with the National Statistic Registry, the distributions of both educational level and income of the parents were representative of Denmark. Likewise, the BMI of both sexes did not differ from the age-specific BMI from school survey data (22). Due to a limited number of accelerometers available to the study, only 427 children had their activity recorded. Of these 427 children, 384 (179 boys and 205 girls) had valid physical activity data, as determined by the criteria described in RESEARCH DESIGN AND METHODS. Of the remaining 43, data were unavailable due to download error ($n = 9$) or were excluded due to instrument breakage ($n = 23$), too little registered time ($n = 10$), or distinct nonphysiological pattern (>9 SDs away from the median physical activity, $n = 1$). The number of children meeting the criteria of exhaustion in the fitness test was 539 (258 boys and 281 girls). Biochemistry data were complete in 525 children, of whom 503 (234 boys and 269 girls) had BP, body composition, and sexual maturation data. A complete dataset of sexual maturation, ethnicity, socioeconomic grouping, parental smoking, physical activity, and the components of the metabolic syndrome was available in 318 children, of whom physical fitness was available in 301 children (145 boys and 156 girls). There were significantly more Caucasians in subgroups of greater data completeness, whereas there was no evidence of differential dropout for the remaining variables. Table 1 displays the descriptive data of all measured variables. None of the children had reached Tanner stage 4 or 5. Median fasting glucose was 5.1 mmol/l, ranging from 4.1 to 6.1 mmol/l.

Bivariate associations

The metabolic syndrome score was inversely correlated with physical activity, fitness, and socioeconomic grouping of the father ($P \leq 0.038$). Positive relationships were found for weight, height, and sexual maturation ($P < 0.001$). Additionally, physical activity was positively related to fitness and inversely related to insulin and triglycerides ($P \leq 0.001$). Fitness was positively related to HDL cholesterol, age, and socioeconomic group of the father but inversely related to weight, height, sexual maturation, adiposity, insulin, triglycerides, and parental smoking ($P \leq 0.021$).

Association between physical activity, fitness, and features of the metabolic syndrome

Physical activity was inversely associated with the standardized scores of insulin ($P = 0.018$) and borderline significantly associated with triglyceride ($P = 0.052$), when adjusting for all confounding factors, but there was no evidence of associations with glucose ($P = 0.123$), HDL cholesterol ($P = 0.174$), systolic BP ($P = 0.357$), diastolic BP ($P = 0.604$), or skinfold thickness ($P = 0.919$). Physical fitness was inversely associated with insulin, triglycerides, systolic BP, and skinfold thickness ($P \leq 0.033$), positively associated with HDL cholesterol ($P = 0.002$), whereas there were no significant associations with glucose ($P = 0.319$) or diastolic BP ($P = 0.765$) following adjustment for all confounding factors.

The physical activity regression coefficients for adjusted models of the metabolic syndrome are displayed in Table 2. Physical activity was inversely associated with metabolic syndrome after adjust-

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Table 1—*Baseline characteristics of Danish 9- to 10-year-old children in the European Youth Heart Study*

Variable	All	Boys	Girls
n	589	279	310
Age (years)	9.6 ± 0.4	9.7 ± 0.4	9.6 ± 0.4
Ethnicity (Caucasian/other)	543/40	258/19	285/21
Weight (kg)	33.6 ± 6.4	34.0 ± 6.4	33.2 ± 6.3
Height (m)	1.39 ± 0.06	1.39 ± 0.06	1.38 ± 0.06
Tanner stage (1/2/3)	490/85/5	275/0/0	215/85/5*
Sum of four skinfolds (mm)	36.8 ± 18	34.1 ± 17	39.2 ± 19*
Insulin (pmol/l)	55.8 ± 33	52.5 ± 36	58.8 ± 29*
Glucose (mmol/l)	5.12 ± 0.4	5.18 ± 0.4	5.06 ± 0.4*
Triglycerides (mmol/l)	0.84 ± 0.3	0.80 ± 0.3	0.89 ± 0.3*
HDL cholesterol (mmol/l)	1.48 ± 0.3	1.52 ± 0.3	1.45 ± 0.3*
Systolic BP (mmHg)	104.9 ± 7.5	105.8 ± 7.6	104.2 ± 7.4*
Diastolic BP (mmHg)	62.9 ± 5.6	63.1 ± 5.7	62.7 ± 5.4
Metabolic syndrome (*Z* score)	0 ± 0.5	−0.07 ± 0.5	0.07 ± 0.5*
Parental smoking (yes/no)	341/231	159/118	182/113
Socioeconomic group			
Mother	2.6 ± 0.9	2.6 ± 0.9	2.6 ± 0.9
Father	3.1 ± 1.0	3.0 ± 1.0	3.1 ± 1.0
Physical fitness (W/kg)	2.99 ± 0.6	3.18 ± 0.6	2.82 ± 0.5*
Physical activity (cpm)	660 ± 233	728 ± 239	600 ± 211*

Data are means ± SD. *$P < 0.05$ for sex difference.

ment for potential confounders, but this relationship was attenuated and nonsignificant when also adjusting for fitness. Excluding level of adiposity from the metabolic syndrome score and adjusting for it as a covariate improved the strength of the relationship between physical activity and metabolic risk but weakened relationships for fitness, although this variable maintained significance in all relevant models ($P \leq 0.031$). Adjusting for BMI instead of skinfold did not alter the results and neither did excluding glucose from the calculation of the metabolic syndrome score (data not shown).

Modification by fitness of the relationship between physical activity and metabolic syndrome was investigated by including an interaction term (physical activity × fitness) in the regression models. A significant interaction was observed for the metabolic syndrome, and a borderline significant ($P = 0.092$) interaction was observed for the metabolic risk score without adiposity. In both models, the noninteraction terms for physical activity and fitness were all significantly negative ($P \leq 0.031$). In the interaction model for metabolic syndrome, the standardized coefficients (95% CI) for physical activity, fitness, and their interaction were −0.071 (−0.138 to −0.003), −0.216 (−0.283 to −0.150), and 0.054 (0.014–0.094), respectively. This is illustrated for quartiles of activity in strata below and above median fitness in Fig. 1.

CONCLUSIONS — The relationship between physical activity and clustering of metabolic risk factors was investigated in a population sample of Danish pre- or early pubertal children. Physical activity was significantly related to metabolic risk, after adjustment for potential confounding factors. Furthermore, we observed a significant interaction between physical activity and fitness, suggesting a stronger relationship between activity and metabolic risk, in children with low cardiorespiratory fitness.

None of the children in this study was diagnosed with metabolic pathology. The metabolic syndrome *Z* score, which we used to define metabolic risk clustering on a continuous scale, is statistically more sensitive and less error prone by comparison to dichotomous approaches (18). The *Z* score should correlate well with the true level of metabolic risk because its subcomponents are measured relatively precisely. In contrast to metabolic syndrome, the primary exposure, habitual physical activity, is highly variable not only between but also within individuals, especially in the pediatric population, which makes it more difficult to measure accurately. Nevertheless, physical activity in this study is probably measured with substantially greater precision than subjective methods (8–11,23) and has been shown to be reliable in this age-group (24). The limitations of the CSA pertain

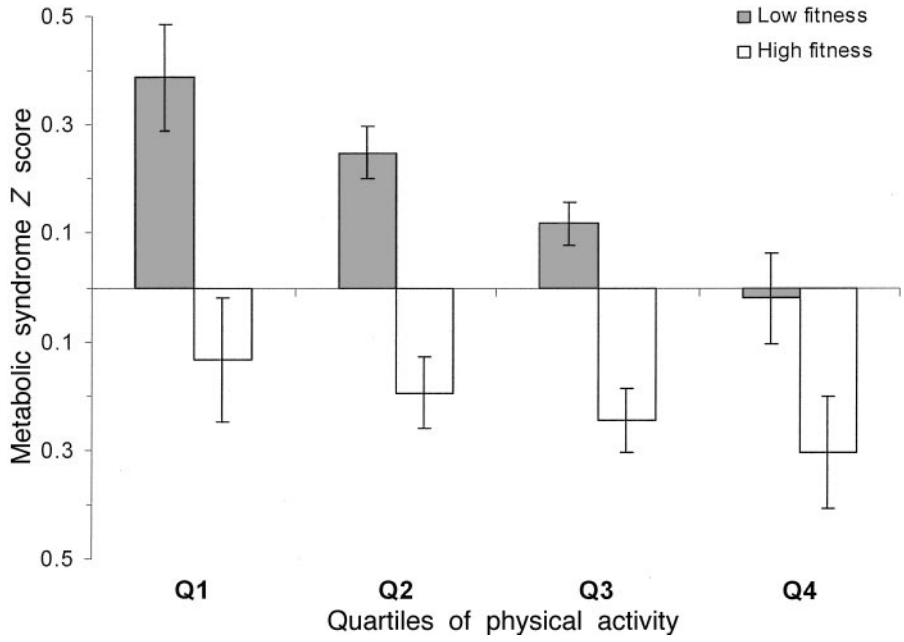

Figure 1—*Relationship between quartiles (Q1–Q4) of physical activity and metabolic risk score (±SE), stratified by physical fitness below (▨) and above (□) the median. Means are adjusted for all covariates.*

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mainly to its inability to adequately capture cycling and swimming activity and the inverse relationship that exists between CSA output and movement frequency (20,25,26). As body size is the most significant determinant of movement frequency (27,28) and because body size is not only closely related to one component of the metabolic syndrome, adiposity, but also sexual maturation, which again is related to most features of the metabolic syndrome, this type of bias would dilute the relationship between physical activity and metabolic risk (negative confounding). It was reassuring, therefore, to observe that the inverse relationships in the bivariate analysis between activity and metabolic syndrome persisted after adjustment for potential confounders, not including fitness. Because uni-axial accelerometers underestimate higher running intensities (25,26), it is likely that this error is most evident in fit individuals who may spend more time running. This type of bias may be one explanation for the weaker relationships in the fitness-adjusted models and may also explain why we observed interactions between activity and fitness. This, however, is complicated by the fact that physical activity and fitness are measured with different degrees of precision, mainly because fitness is much less variable within individuals than habitual physical activity (29). Thus, it is difficult to judge the true relative importance of habitual physical activity over fitness. In a recent study (7) of U.K. Caucasian adults, a similar interaction between activity and fitness on metabolic risk clustering was observed even after correction for differential measurement error in the exposures of activity and fitness. The nature of this interaction was very similar to that observed in the present study of Danish children. Since physical activity in the U.K. study was measured by 4 days of heart-rate monitoring, the argument that the interaction between activity and fitness could be generated by measurement error specific to the CSA is substantially weakened and adds credibility to the interpretation of the present data that physical activity is related to metabolic risk in children and that this relationship may be modulated by fitness level.

Using doubly labeled water data (23), we were able to ascertain that an increase of 1 activity unit (transformed square root of counts per minute scale) corresponds to an increase of 6.49 kJ/kg of daily physical activity energy expenditure (age and sex adjusted). In the present study, the nonfitness-adjusted physical activity coefficients were around −0.02. Therefore, to decrease the metabolic *Z* score by 1/10 of a unit would require an additional 32 kJ/kg of energy expenditure through physical activity. For an average 10-year-old child weighing 32 kg, this would correspond to about 1 extra megajoule of energy expenditure per day. One megajoule more per day is a substantial increase in energy expenditure in exchange for a relatively small decrease in the metabolic syndrome score. However, we observed this dose-response relationship in a population-based sample of healthy children. As metabolic risk factors are known to track over time, these relatively small effects may translate into significant reductions in the occurrence of disease later in life (5,30,31). Moreover, these effects may be greater in high-risk individuals, e.g., less fit children or indeed less fit adults (7). In the cohort of children below median fitness level, the same 1/10-unit reduction on the metabolic syndrome score could be achieved with only 15 kJ/kg of extra energy expenditure.

The relationships we report here in Danish children are supported by observations in the Cardiovascular Risk in Young Finns Study (32), which demonstrate significant inverse relationships between physical activity with subscapular skinfold thickness and triglycerides. In males only, there were additional beneficial effects of activity on insulin and HDL cholesterol, whereas BP was unrelated to activity in either sex. This was also observed in longitudinal analyses, when considering persistent activity (tracking) as the exposure (33). The role of activity in clustering of metabolic risk factors is also supported by the observation of a stronger relationship between activity and insulin sensitivity in high-BP individuals (34). In a North Irish longitudinal study, fitness (at ages 12 and 15 years) was a predictor of total–to–HDL cholesterol ratio and sum of four skinfolds but not BP at age 22.5 years, but there was no relationship between any of the three risk factors and self-reported activity at ages 12 and 15 years (35). This corresponds well with our observation that the relationships between activity and these three risk factors were not significant. Most of the variation in the metabolic risk score

Table 2 —*Prediction of the metabolic syndrome score by physical activity and fitness*

	Metabolic syndrome *Z* score including adiposity			Metabolic syndrome *Z* score excluding adiposity*		
	PA coefficient (standardized)	95% CI	*P*	PA coefficient (standardized)	95% CI	*P*
Model A: adjusted for age, sex, ethnicity, sexual maturation, parental smoking, and socioeconomic group of each parent	−0.020 (−0.092)	−0.035 to −0.006	0.008	−0.025 (−0.115)	−0.043 to −0.008	0.005
Model B: model A, additionally adjusted for fitness	−0.012 (−0.053)	−0.027 to 0.004	0.127	−0.020 (−0.089)	−0.039 to −0.000	0.045
Model C: model B, including interaction term	−0.078 (−0.071)	−0.129 to −0.028	0.004	−0.071 (−0.102)	−0.135 to −0.007	0.031
Interaction	0.021 (0.054)	0.006–0.036	0.010	0.016 (0.042)	−0.003 to 0.035	0.092

Data are absolute β-coefficients (standardized values) or 95% CIs. Average CSA cpm was normalized by square root. Ninety-five percent CIs were obtained with robust SEs by clustering on school. *All models of nonadiposity metabolic syndrome are additionally adjusted for adiposity as an exposure. PA, physical activity.

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that can be explained by physical activity is attributable to reductions in fasting insulin and triglycerides, but these risk factors were not measured in the North Irish study, and the interaction with fitness was not explored (35). Similar observations were reported in an American study (36) in which fitness was inversely related to LDL–to–HDL cholesterol ratio, BMI, and BP, whereas activity was associated only with lower BMI. Only a single study (37) has reported a positive relationship between doubly labeled water–measured energy expenditure and insulin levels, although this could be explained by extreme values in two outliers. Moreover, since this analysis was not adjusted for body size, sexual maturation, or adiposity, the positive association may be attributable to confounding.

Intervention studies in children have demonstrated the utility of increased physical activity to improve metabolic regulation after 3 weeks of daily exercise and low calorie diet (38) and to reduce BP after 8 months following three additional physical education lessons per week (39). Four months of training (5 × 40 min/week) resulted in significant decreases in insulin, triglycerides, and body fat but no changes in glucose and HDL cholesterol in 79 obese children (40). Moreover, the improvements in metabolic profile that corresponded with exercise training had regressed back to baseline values after 4 months of no exercise facilitation, thus supporting the etiological role of physical activity. A 10-week intervention study (41), in which obese girls were assigned to either lifestyle education or facilitated physical training, showed decreases in triglycerides, HbA_{1c}, and total–to–HDL cholesterol ratio but not in fasting insulin, glucose, or HDL cholesterol. However, only vigorous activity increased in the two intervention groups, whereas overall activity remained at the same level. This kind of compensation was also observed in another training study in adolescents (42), which demonstrated favorable changes in triglyceride level, total–to–HDL cholesterol ratio, and diastolic BP but no changes in insulin, glucose, adiposity, or systolic BP. When training attendance was considered, significant decreases in triglyceride, total–to–HDL cholesterol ratio, and adiposity were observed, along with a trend for decreased insulin. Furthermore, there was a more pronounced effect of the physical training program on lipid profile if baseline values were high in both the intent-to-treat and attendance-rate adjusted analyses, indicating greater effect in high-risk individuals (42).

Although the cross-sectional nature of our study limits inference about the direction of causality, it is biologically plausible that physical activity improves the metabolic risk profile. Firstly, insulin action and glucose transport may be enhanced (43,44). Secondly, increased capillarization results in increased blood flow and oxygen supply to the muscle tissue, which results in improved fat metabolism, higher HDL cholesterol levels, and decreased BP (43,45–59). Thirdly, overall sympathetic tone and thus BP may decrease through a more efficient recruitment of the motor units in the muscle (60–62).

In conclusion, clustering of metabolic risk factors is inversely related to physical activity in pre- or early pubertal children. These observations are unlikely to be explained by chance, bias, or confounding; are consistent with other studies; and are biologically plausible. This suggests that children, particularly those who are less fit, should be encouraged to engage in physical activity to improve their metabolic health and to establish healthy habits.

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