The relationship between physical activity level and cardiovascular disease biomarkers in healthy, normal-weight 3-to 6-year-old children and their parents

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BRIEF COMMUNICATION

The relationship between physical activity level and cardiovascular disease biomarkers in healthy, normal-weight 3- to 6-year-old children and their parents

Carol Huang, Marja Cantell, Susan Crawford, Deborah Dewey, and Danièle Pacaud

Abstract: To determine if physical activity is linked to cardiovascular biomarkers in preschool children at risk, we need information on these biomarkers in healthy normal-weight children. In this population, multi-level modelling analyses found no correlation between accelerometer recorded physical activity and fasting lipids, adiponectin, or insulin sensitivity. Exploratory analyses found positive correlations between adiponectin and time spent in light physical activity, and between triglyceride and time spent in sedentary behaviour; these findings need to be confirmed in longitudinal prospective studies.

Key words: physical activity, preschool children, cardiovascular disease biomarkers, parent-child triad, body mass index.

Résumé : Cette étude se propose de déterminer si l'activité physique est liée à des biomarqueurs chez des enfants d'âge préscolaire à risque. Pour le savoir, on doit analyser les biomarqueurs chez des enfants en bonne santé et de poids normal. Dans cette population, l'analyse par modélisation multiniveaux ne révèle aucune corrélation entre l'activité physique mesurée par accélérométrie et les lipides à jeun, l'adiponectine et la sensibilité à l'insuline. Des analyses exploratoires révèlent des corrélations positives entre l'adiponectine et le temps consacré à des activités physiques d'intensité légère et entre les triglycérides et le temps consacré à des activités sédentaires; ces observations restent à confirmer par des études prospectives longitudinales. [Traduit par la Rédaction]

Mots-clés : activité physique, enfants d'âge préscolaire, biomarqueurs des maladies cardiovasculaires, triade parents-enfant, indice de masse corporelle.

Introduction

Cardiovascular disease (CVD) is one of the most important causes of morbidity and mortality in modern society, and risk factors for CVD include obesity, insulin resistance, hypertension, and dyslipidemia. Many of these CVD risk factors are present in childhood, especially in school-aged obese children and adolescents, and they often persist into adulthood (Jensen et al. 2014). Adiponectin is a CVD biomarker with insulin sensitizing, antiatherosclerotic, and anti-inflammatory effects and it forms trimeric (LMW), hexameric (MMW), and oligomeric (HMW) complexes in the circulation; HMW adiponectin is the physiologically active isoform with the best predictive value for CVD risk and type 2 diabetes (Araki et al. 2006; Jensen et al. 2014). In overweight and obese older children, serum lipid and total adiponectin levels are modifiable by lifestyle programs (Cambuli et al. 2008). However, little is known about these biomarkers in preschool-aged children of normal weight. Further, as physical activity is negatively associated with adiposity (Collings et al. 2013), it is pertinent to consider its relationship with CVD biomarkers in normal-weight children of preschool age. Using data collected as part of a longitudinal observational study on physical activity in preschool-aged children and their parents (Cantell et al. 2012), this study investigated the relationships between level of physical activity and serum levels of CVD biomarkers in a group of healthy, normal-weight preschool children.

Materials and methods

Participants

As part of the Y-Be-Active study, a community sample of 54 families with preschool-aged children were recruited. The sociodemographic characteristics of the sample are reported in Supplementary Table SI[1] (Cantell et al. 2012).

To address the purpose of the current study, the baseline data on CVD biomarkers and anthropometry from parent–child triads was used. Families met the following criteria: (*i*) a healthy 3- to 6-year-old child with no physical/mental disability that would interfere with participation in physical activity; and (*ii*) 2-parent family with both parents residing in the home. In families with

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[1]Supplementary data are available with the article through the journal Web site at http://nrcresearchpress.com/doi/suppl/10.1139/apnm-2016-0023.

more than 1 child participating in Y-Be-Active, 1 child was randomly selected. As the Y-Be-Active study was interested in examining possible genetic association between parents' and children's CVD biomarkers, adopted children were excluded. The study was approved by the Conjoint Health Research Ethics Board of the University of Calgary.

Measurements

CVD biomarkers

Fasting blood samples were obtained. Serum total cholesterol, triglycerides, and high-density lipoprotein (HDL) was measured by the CHOD-PAP enzymatic colorimetric assay, the enzymatic colorimetric assay, and the HDL-C Plus Colorimetric Assay (Roche Diagnostics, Cobas 6000, Rotkreuz, Switzerland), respectively. Apolipoprotein A1, apolipoprotein B1, and lipoprotein (a) were measured by the nephelometric assay (Dade Behring, Deerfield, Ill., USA). Total and high molecular weight adiponectin levels and insulin levels were determined with the Adiponectin (multimeric) or the Insulin ELISA kits (ALPCO, Salem, Ore., USA). Homeostatic model assessment of insulin resistance was calculated from the insulin and fasting glucose measure using the following formula:

$$(\text{glucose} \times \text{insulin})/22.5$$

where glucose is in mmol/L and insulin is in μIU/mL.

Physical activity

Physical activity was measured using the ActiGraph 7146 accelerometers, which has been validated for children <5 years of age. The accelerometer was worn by children and parents for 5 consecutive days (3 weekdays, 2 weekend days), a duration necessary to achieve a reliability level of 0.80 (Cliff et al. 2009). Accelerometer data were validated against an activity diary and included only if the accelerometer was worn for at least 9 h for weekdays and 6 h for weekend days. On average, children wore the accelerometers 11.8 ± 1.3 h/weekday and 10.6 ± 2.4 h/weekend day. The accelerometers sampled physical activity at 1-min intervals to ensure that our measure of physical activity was the same for parents and children. Levels of physical activity were categorized as sedentary (SPA) (<500 counts of movement/min), light (LPA) (≥500 but <1680 counts of movement/min), and moderate or vigorous physical activity (MVPA) (≥1680 counts of movement/min) (Cantell et al. 2012). Time spend in vigorous physical activity and moderate physical activity were combined and reported as MVPA to address the potential misclassification of vigorous activity as moderate activity when using 1-min epochs (Cliff et al. 2009; Metcalf et al. 2009).

Anthropometry

Height, weight, and waist girth were measured as previously described (Cantell et al. 2012). Briefly, waist circumference was measured with the child standing, horizontally at the midpoint between the 10th rib and the iliac crest (Taylor et al. 2008). All measurements were taken 3 times and the mean of the 2 closest values was recorded. Body mass index (BMI) (weight (kg)/height (m^2)) for age and sex was calculated for the children and their parents (Supplementary Table SI[1]).

Questionnaires

Parents completed questionnaires on family sociodemographics (Supplementary Table SI[1]). Socioeconomic status (SES) was measured using the Blishen Index (Blishen et al. 1987), which is a Canadian measure of socioeconomic status. For each family, the occupation of the parent with the highest SES on this index was used as the indicator of family SES.

Statistical analyses

Multi-level modelling was conducted to examine the relationships among physical activity and biomarkers, while controlling for individual factors (e.g., sex, age) and the family of each participant. Exploratory analyses of relationships between CVD biomarkers and physical activity in preschool children and relationship between CVD biomarker levels of children and their mothers and fathers were performed using a series of Pearson r correlations and Spearman correlations where appropriate. Statistical analyses were carried out using IBM SPSS for Windows (version 19; IBM Corp., Armonk, N.Y., USA). Results are significant at $p < 0.05$.

Results

Findings on physical activity level of the children and the relationship between parent–child physical activity have been published and baseline results are summarized in Supplementary Table SI[1] (Cantell et al. 2012). This group of children spent most of their time in SPA or LPA, and most attained 60 min of daily MVPA on weekdays. Only 60% of fathers and approximately one-half of mothers attained 30 min of daily MVPA. Although only 22% of children were enrolled in full-time daycare, the level of physical activity attained did not differ between children cared for at home or in daycare.

In the children, the multi-level modelling analysis revealed no significant relationships between CVD biomarkers and MVPA (Supplementary Table SII[1]). As multi-level modelling could have masked associations that may be of interest, given our small sample size, we conducted exploratory analyses of these relationships. As shown in Supplementary Fig. 1*a*[1], for the children, a positive correlation was found between total adiponectin and percentage of time spent in LPA on weekdays ($r = 0.417$, $p < 0.05$); the association between HMW adiponectin and LPA on weekdays ($r = 0.310$, $p = 0.09$) is also shown (Supplementary Fig. 1*b*[1]). Higher triglyceride levels were correlated with more time spent in sedentary behaviour during weekdays ($r = 0.307$, $p < 0.05$) (Supplementary Fig. 1*c*[1]). When the effects of children's age and BMI were partialled out, there was a positive correlation between higher apolipoprotein A1 and percentage of time spent in MVPA ($r = 0.629$, $p < 0.05$). For boys, fasting blood glucose negatively correlated with LPA ($r = -0.762$, $p < 0.05$) and positively correlated with sedentary behaviour ($r = 0.579$, $p < 0.05$). No significant correlations were found between the children's biomarkers, MVPA, BMI, and waist circumference (Supplementary Table SIII[1]).

Since family history is a significant determinant of CVD risk, we correlated children's and parents' CVD biomarkers (Table 1). We found significant positive correlations between children's and mothers' total cholesterol, low-density lipoprotein (LDL), HDL ratio (i.e., HDL/total cholesterol), Apolipoprotein (A-1), Apolipoprotein (B), and lipoprotein (a). Between the child and the father, we found a significant correlation for fasting glucose levels only. When we adjusted for level of physical activity, the results remained unchanged.

Discussion

Many risk factors for CVD originate in childhood, and a better understanding of predictive factors for CVD risk will allow for the design of preventative measures in childhood (Magnussen et al. 2013). This is a unique study because we collected physical activity data using accelerometers on 54 parents–child triads. The small sample size and the lean nature of the preschool aged children may have resulted in the multi-level modelling analysis not revealing any relationship between CVD biomarkers and physical activity levels in the children. However, our exploration of potential associations, which could aid in the design of a larger, fully powered study, revealed positive correlations between the time children spent in sedentary behaviour and higher triglycerides,

Table 1. Biomarkers for children and parents.

Biomarkers	Mothers	Fathers	Child	Correlation between child and mother	Correlation between child and father
Fasting glucose (mmol/L)	5.37±2.37	5.15±0.49	4.71±0.35	$r = 0.342$, $p = 0.088$	$r = 0.70$, $\mathbf{p = 0.002}$
Fasting insulin* (μIU/mL)	7.28±5.64	7.89±6.92	9.24±17.34	$r = 0.244$, $p = 0.221$	$r = -0.142$, $p = 0.562$
HOMA-IR	1.98±2.15	1.93±1.29	0.92±0.67	$r = -0.087$, $p = 0.766$	$r = -0.147$, $p = 0.666$
Total cholesterol (mmol/L)	4.62±1.38	4.66±1.05	3.99±0.79	$r = 0.719$, $\mathbf{p < 0.001}$	$r = 0.217$, $p = 0.288$
Triglycerides (mmol/L)	1.06±0.81	1.25±0.86	0.72±0.25	$r = 0.225$, $p = 0.168$	$r = 0.326$, $p = 0.104$
LDL (mmol/L)	2.63±1.34	2.74±0.91	2.19±0.78	$r = 0.753$, $\mathbf{p < 0.001}$	$r = 0.305$, $p = 0.130$
HDL (mmol/L)	1.53±0.37	1.34±0.17	1.47±0.32	$r = 0.305$, $p = 0.059$	$r = 0.059$, $p = 0.773$
HDL ratio (HDL/total cholesterol)	3.17±1.08	3.53±0.96	2.84±0.89	$r = 0.522$, $\mathbf{p = 0.001}$	$r = 0.241$, $p = 0.235$
Apolipoprotein (A-1) (g/L)	1.51±0.24	1.41±0.20	1.36±0.19	$r = 0.374$, $\mathbf{p = 0.023}$	$r = -0.079$, $p = 0.714$
Apolipoprotein (B) (g/L)	0.84±0.28	0.84±0.27	0.72±0.19	$r = 0.598$, $\mathbf{p < 0.001}$	$r = 0.374$, $p = 0.078$
Lipoprotein (a) (g/L)	0.19±0.24	0.13±0.16	0.11±0.16	$r = 0.428$, $\mathbf{p = 0.008}$	$r = 0.218$, $p = 0.318$
Total adiponectin (μg/mL)	5.86±2.1	4.63±1.77	8.24±2.55	$r = -0.091$, $p = 0.667$	$r = -0.086$, $p = 0.751$
HMW adiponectin (μg/mL)	3.41±1.55	2.22±1.50	4.96±2.02	$r = -0.153$, $p = 0.465$	$r = 0.156$, $p = 0.564$

Note: Biomarker data are presented as means ± SD. Bold text indicate changes that are statistically significant. HDL, high-density lipoprotein; HMW adiponectin, high molecular weight adiponectin; HOMA-IR, homeostasis model of assessment - insulin resistance; LDL, low-density lipoprotein.

*Spearman's correlation was performed for fasting insulin as it is a non-normally distributed variable. Pearson correlation was performed for all other biomarkers.

and between higher levels of physical activity and higher serum levels of adiponectin.

Adiponectin is secreted by the adipocyte and a low adiponectin level is associated with CVD, hypertension, and metabolic syndrome (Jensen et al. 2014). Here, we found a positive correlation between physical activity and total adiponectin, and to a lesser degree, the more physiologically relevant HMW adiponectin. Interestingly, both positive (Cambuli et al. 2008) and negative correlations (Metcalf et al. 2009; Emken et al. 2010) between serum adiponectin levels and physical activity have been reported. Emken et al. (2010) suggested that physical activity upregulates adiponectin receptor, hence reduced the need for high levels of serum adiponectin. Metcalf et al. (2009) found this negative correlation only in the least physically active group, suggesting that when physical activity is too low to maintain insulin sensitivity, adiponectin level increases to compensate. The higher level of MVPA attained by the preschool children in our study as compared with school-aged children (Colley et al. 2011; Cantell et al. 2012) may have been sufficient to influence metabolism during LPA and explain the positive correlation between LPA and adiponectin found in our study. These conflicting results are likely due to variations in the age, pubertal stage, and BMI of the study populations.

Relationships among physical activity and other CVD risk markers such as HDL, triglycerides, LDL, glucose, and insulin levels have been reported in older children (Raitakari et al. 1997; Katzmarzyk et al. 1999). Here, we observed a positive correlation between serum triglycerides and time spent being sedentary, suggesting that in normal-weight, 3- to 6-year-old children, being sedentary may contribute to adverse lipid profiles.

Interestingly, while studies in obese children have reported a significant relationship between BMI and CVD risk markers (Magnussen et al. 2013), we did not find significant correlations between the children's BMI and CVD biomarkers, or their BMI and physical activity levels. This could be due to the rather lean phenotype of the children in our study. In children with a wider BMI range, Saakslahti et al. (2004) reported a negative correlation between BMI and self-reported physical activity level while Vorwerg et al. (2013) found no correlation between BMI and accelerometer-recorded physical activity levels.

To determine the contribution of family history to serum levels of biomarkers (Al-Daghri et al. 2011), we analyzed the associations among CVD biomarkers in children and their parents. While we found only 1 significant correlation between children's and fathers' biomarkers, i.e., fasting glucose, we found significant correlations between several of the children's and mothers' biomarkers. Interestingly, our previous report found that higher level of MVPA activity in fathers was associated with higher MVPA in their children (Cantell et al. 2012). Therefore, the lack of a significant relationship between fathers' and children's biomarkers suggests that the association between the children's and mothers' biomarkers are either related to shared diet during the week, or a more pronounced maternal genetic influence on children's biomarkers.

The strength of this study is in the objective measurement of physical activity by accelerometer in the parent–child triad. One limitation is the high SES of the participants, which may limit the generalizability of results, although low SES has been shown to associate with more screen time but not lower physical activity (Tandon et al. 2012). The relative racial homogeneity of our sample may also limit the study results to similar racial groups, but it was representative of background population where the study was conducted (StatCan 2007). Another limitation is sample size. Nevertheless, our exploratory analyses revealed correlations between the children's physical activity level and CVD risk markers, and between children's and mothers' lipid levels, information that will be useful in the design of a fully powered study.

In conclusion, we found that in healthy, normal-weight, 3- to 6-year-old children, physical activity levels do not correlate with CVD biomarkers. However, further exploratory analysis revealed that both total and HMW adiponectin were positively associated with physical activity, and children's and mother's lipid levels were correlated. These findings suggest that in very young children of normal weight, both physical activity levels and hereditary factors may be important determinants of their cardiometabolic risk markers. Longitudinal prospective studies are needed to investigate whether interventions that change physical activity levels positively influence CVD biomarkers and reduce CVD risks in young, at-risk pediatric populations.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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mentary Table SI[1], which include the age of the children and their parents, as well as the BMI of the parents, were already published in the aforementioned study.

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