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Editorial

A little more time around the track may go a long way: Implications of increasing moderate to vigorous physical activity in pre-adolescents

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In an attempt to combat the global burden of cardiovascular disease (CVD), Valentin Fuster's research group has demonstrated that successful lifestyle modifications can be taught to and implemented in children as young as preschool age [1,2]. This has bolstered hope that primordial prevention of CVD can be applied very early on and lead to overall improved population health as these children become adults. For those children beyond the 3–5 year age range, however, there is still a significant role for improving modifiable CVD risk factors. Physical activity (PA) and dietary modifications are the most common targets for interventions in children as well as adults, with the benefit that unlike adults, children in school systems may be more amenable to intervention programs focusing on these factors.

Indeed, the field of PA as it relates to CVD risk related metabolic profiles in children has been active for about forty years. While it is well known that decreased PA is associated with increased obesity and cardio-metabolic risk factors in youth [3–5], given multiple different study designs and measures, the optimal intensity or duration of exercise needed for long-term benefit is still unknown [3,6–8]. In addition, what may be optimal in preschoolers may not apply as children enter and travel through adolescence into early adulthood. The relationship of PA with age and sex, additionally, needs to be studied further, as we start recommending interventions at increasingly younger ages.

In this issue of *Atherosclerosis,* authors Jones et al. assess the cross-sectional association between detailed lipoprotein profiles measured by nuclear magnetic resonance (NMR) spectroscopy with levels of PA and sedentary time in children enrolled in the Active Smarter Kids (ASK) study, to better understand the mechanisms by which PA may improve multiple metabolic parameters [9]. Prior findings from the same research group demonstrated that moderate to vigorous PA (MVPA) is prospectively and inversely associated with cardiometabolic risk factors in otherwise healthy children. In contrast, sedentary time in children appeared to be unrelated to individual or clustered risk (where clustered risk relates to clusters of risk factors found in subgroups of otherwise healthy children) [8,10]. How the lipoprotein profiles in children relate to associations with PA and sedentary time, illustrates the novel aspects of this study.

Triglyceride-rich lipoproteins (TRLPs) comprise a spectrum of lipoprotein subfractions, namely chylomicrons, very low-density lipoprotein (VLDL), and intermediate density lipoprotein (IDL). In the 1970s, Zilversmit, one of the early proponents of TRLP related risk, conducted a series of animal studies suggesting that increased levels of and prolonged arterial exposure to TRLPs, specifically chylomicron remnants and VLDL, may be causally related to subsequent atherogenesis in the arterial intimal wall [11,12]. Recently, investigation of TRLP related risk has experienced a renaissance, with studies now demonstrating that increased TRLP levels confer increased CVD risk independently of low-density lipoprotein cholesterol (LDL-C) levels or LDL-C reduction [13]. In addition, genetic studies suggest that lifelong high plasma concentrations of TRLPs or their remnants are causally related to an increased risk of coronary heart disease [14]. In this regard, the effect of exercise on lipoprotein subfractions is of key interest and has been previously studied in adults. A relatively recent meta-analysis by Sarzynski et al. assessed NMR spectroscopy measured lipoprotein subfractions from 6 different exercise intervention studies in adults (10 different interventions in total) and concluded that regular physical activity shifts lipoprotein subfractions into a more favorable pattern with respect to CVD risk. In that analysis, large sized VLDL particle concentration and small sized LDL particle concentrations were decreased whereas large sized HDL and LDL particles were increased with regular exercise (at least 3 sessions/week of minimum 50% VO2 max intensity) [15] Furthermore, studies in apparently healthy adult populations have found this particular lipoprotein pattern (that is modified by PA) to be related to future cardiovascular events [16].

The authors of the present study sought to assess if similar favorable patterns were associated with MVPA in otherwise healthy children

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participating in the ASK study. The ASK study was a seven month cluster randomized controlled trial designed to assess the effect of PA interventions in a school setting on academic performance and different health indices in consenting 5th grade, Norwegian school children [17]. It is important to note that the study design for the present analysis was cross-sectional and not longitudinal, as in the original trial. All blood samples were drawn at baseline before any exercise intervention and similarly accelerometer data was also obtained at baseline. Well known, Evenson cutpoints were used to categorize accelerometer measured baseline activity level into sedentary time ($\leq$100 counts/min), light physical activity ($>$ 100 to $<$ 2296 counts/min) and MVPA ($\geq$2296 counts/min). Since the authors were interested in the effect of exercise, PA variables were further defined in terms of unit increments; where one-unit increment represented 30 minutes of activity of any type. In addition, prior to regression analysis, lipoprotein measures were scaled to standard deviation (SD) units such that the regression coefficients presented represent an SD unit increment in lipoprotein measures per unit (30-min) increment in PA. Finally, time-use data, such as that used in this study, are limited to a total number of hours per day and so durations of sedentary behavior and physical activity constitute proportions of a complete day. In statistical terms, time-use data such as PA can be considered compositional data. Compositional isotemporal substitution is a method applied to estimate change in a health outcome when fixed durations of time are reallocated from one particular time-use composition component to another. In this form of analysis, remaining components are kept constant based on a multiple linear regression model on isometric log ratio coordinates [18]. In this present study, isotemporal substitution was used to model how replacing 30 minutes of sedentary time with 30 minutes of MVPA may affect the cross-sectional association with lipoprotein measures, likely as a way to further guide physical activity recommendations for school aged children.

In general, the authors' findings support their conclusion that higher levels of PA were associated with more favorable lipoprotein profiles in the student participants of this study, independent of sedentary time. Most notably, the predominant favorable associations with MVPA were in decreased levels of apolipoprotein-B containing particles, in particular, the TRLP chylomicrons and VLDL subfractions. After adjusting for adiposity, the results somewhat attenuated although small inverse associations remained between MVPA and several TRLP measures (including large and medium sized VLDL particle concentrations, among others). At the same time, larger average LDL and high-density lipoprotein (HDL) particle sizes were positively associated with MVPA. In addition, medium sized HDL and HDL cholesterol (HDL-C) remained positively associated with MVPA in adiposity-adjusted models. Similar patterns were seen in the isotemporal substitution model.

While it is tempting to infer that MVPA in children has a direct favorable effect on atherogenic lipoproteins, and while this may indeed be true, we cannot conclude this from these particular cross-sectional data. In addition, important lifestyle information such as dietary habits and genetic details are not available for these children. It is possible that those with higher MVPA also had other healthy behaviors such as nutritionally sound overall diets, less television time, and increased cardiorespiratory fitness (the latter two being suggested as independent risk factors in some studies) [3,19] as well as favorable genetic profiles. Some other limitations of the study include the fact that the population is restricted to students in Norway, who were fairly active at baseline. This would limit generalizability somewhat, especially for populations where other negative factors such as air pollution may attenuate benefits conferred by out-door exercise.

Despite the above, this study highlights the important interplay between exercise, adiposity, and lipoprotein metabolism in children. The study had a large sample size and objective, valid method for PA assessment. Furthermore, the results are consistent with expectations based on previous findings in adults. A longitudinal study that addresses the question of dose of MVPA needed in different subgroups and how this translates into adult behavior/health would be challenging but still very much needed. In the meantime, we recommend that both children and adults take more extra runs around the track on a regular basis.

Conflict of interest

Dr. Farukhi has no disclosures.

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