Medicina Sportiva
Med Sport 13 (1): 22-27, 2009
DOI: 10.2478/v10036-009-0005-6

METABOLIC SYNDROME, PHYSICAL ACTIVITY AND ADIPOCYTOKINES IN CHILDREN AND ADOLESCENTS

Toivo Jürimäe[A,E], Jaak Jürimäe[A,F], Jarek Mäestu[A,E]

Faculty of Exercise and Sport Sciences, University of Tartu, Tartu, Estonia

Abstract

Metabolic syndrome is a major risk factor for cardiovascular diseases and type 2 diabetes. Biomarkers of the metabolic syndrome develop early in life and can be predictive of atherosclerotic processes in adulthood. Low physical activity levels in children, with a possible modulating effect of cardiorespiratory fitness have been associated with a higher clustering of metabolic risk factors in adults. All these markers are highly influenced by physical activity level and physical fitness. Evidence suggests that there is a significant genetic component involved in physical fitness phenotypes. However, there are very limited data in the literature on genetic predisposition to physical activity level in children and adolescents. Adipose tissue has now been considered as an endocrine organ that produces many molecules called adipocytokines. Leptin and adiponectin are most studied regarding the metabolic risk factors, while adiponectin is considered as one of the most promising biochemical marker to characterize metabolic syndrome in adults. There are yet no studies that have longitudinally investigated the complex changes of the metabolic risk factors, physical activity and fitness and adipocytokines in children throughout puberty. This review addresses the studies that have been conducted on adipocytokines and physical activity and their possible impact to metabolic syndrome in chilndren and adolescents.

Key words: *metabolic syndrome, physical activity, physical fitness, adipocytokines, children and adolescents*

Metabolic syndrome, physical activity and fitness

Major changes have occurred in developed countries over the past 50 years in lifestyle and physical growth of children and adolescents. Changes in their food consumption and increasingly sedentary lifestyle are accompanied by decreasing participation in sports as children approach maturity. Most youth do not meet minimal physical activity recommendations on a regular basis (1). The prevalence of overweight has increased about threefold in children over the past few decades in the United States and other developed countries have also experienced recent increases in the prevalence of childhood obesity and overweight (1). A significant body of small-scale experimental studies has indicated that the course of this progressively worsening situation can be essentially stopped and even reversed if children maintained a healthy diet with balanced energy intake and consumption, reduced the time on sedentary pursuits, exercised regularly, and maintained a normal body weight.

Metabolic syndrome is a major risk factor for cardiovascular diseases and type 2 diabetes. It is generally considered as the clustering or co-occurrence of biomarkers associated with atherosclerose and insulin resistance, namely elevated levels of abdominal adiposity, blood pressure, triglycerides, glucose, and a low level of high-density lipoprotein–cholesterol (HDL-C). Previous studies have shown that factures of the metabolic syndrome develop early in life and can be predictive of atherosclerotic processes in adulthood (2). Some of the encountered inconsistencies in defining the metabolic syndrome in children can be attributes to growth and body evolution that manifests itself in changes of metabolic and clinical characteristics in pediatric populations (3). In 2007 International Diabetes Federation published consensus statement that may provide a simple definition of easily measurable variables in composing both age and sex specific cut-off points (4,5). There are well defined criteria for metabolic syndrome in 10 to 16 year-olds (e.g. obesity, triglycerides, HDL-C, blood pressure, glucose). However, in view of the metabolic syndrome in children and to some extent also in adults, it has been suggested to focus more on the individual risk factors and less on an aggregation of single indicators (6). Kwiterovich (7) proposed the following definition of metabolic syndrome in adolescents: triglycerides ≥ 110 mg/dL; HDL-C ≤ 40 mg/dL; waist circumference ≥ 90th percentile; fasting glucose ≥ 110 mg/dL and systolic blood pressure ≥ 90th percentile for age, gender and height presence of at least three of the above presented factors. Since there is no universal definition of the metabolic syndrome in children or adolescents, several authors have derived a continuous score representing a

composite coronary vascular disease risk factor profile or index (i.e., the metabolic syndrome score) (8). Large population studies have shown that even though the prevalence of metabolic syndrome in children and adolescents is relatively low (between 3% and 4%) when compared to the adult population (23.7%), there is a high prevalence of metabolic syndrome in overweight and obese adolescents (28.7%) (9).

Recent findings show that the number of adipocytes for lean and obese individuals is set during childhood and adolescence, and that adipocyte numbers for these categories are subject to little variation during adulthood. Even after significant weight loss in adulthood and reduced adipocyte volume, the adipocyte number remains the same (10). There are several recommendations to measure adiposity. Most studies have used body mass index (BMI, kg/m^2) (11). However, visceral or central fat depots have greater metabolic importance. Waist circumference has usually been measured for that purpose. Baumgartner et al. (12) concluded that subcutaneous adipose tissue deposition increases on the trunk in boys during the puberty.

Physical fitnesss activity and metabolic syndrome

The therapeutic role of exercise in the prevention, treatment and control of metabolic disease may involve multiple mechanisms. Physical activity is defined as any bodily movement produced by skeletal muscles that results in energy expenditure above the resting metabolic rate (13). Exercise refers to a specific type of physical activity, which is defined as a planned, structured, and repetitive bodily movement done to improve or maintain physical fitness (14). Despite progress in physical activity assessment, the limitations concerning measurement accuracy are often amplified in young people due to cognitive, physiological and biomechanical changes that occur during matural growth and development (15). Nonlinear modeling techniques to estimate energy expenditure and physical activity mode using accelerometry together with physiological parameters like heart rate or body temperature have the greatest potential for increasing the accuracy of the prediction of energy expenditure of physical activity in children and adolescents (15).

In children and adolescents, physical activity has similarly been found to be favourably associated with several metabolic risk factors and with the risk of metabolic syndrome at young adult age (16,17). The more convincing studies concern insulin sensitivity and dyslipidaemia while the beneficial effects of physical activity on blood pressure have mainly been demonstrated for overweight children and adolescents with hypertension (18). Recently, Platat et al. (19) suggested that regular physical activity is associated with improved insulin sensitivity independently of adiposity and body fat distribution in adolescents. Pan and Prat (20) results in a big group of 12-to-19-year-old Americans support the need to engage adolescents in systematic physical activity and healthful dietary practices to prevent excessive weight gain. Body mass control should be recommended as the first-line intervention to decrease metabolic syndrome in adolescents. Interestingly, Leary et al. (21) revealed that higher levels of physical activity were associated with lower level of blood pressure in 11-12-year-old children, suggesting that the volume of physical activity may be more important than the intensity.

Metabolic syndrome and physical fitness

The term "fitness" is commonly accepted in the exercise science community, as referring to health-related physical fitness (cardiorespiratory, muscular, motor, metabolic, morphological) (22). Rizzo et al. (23) suggested that cardiorespiratory fitness is more correlated to metabolic risk than total physical activity. This causal connection is explained by the pivotal role of body fat in the association of cardiorespiratory fitness with the metabolic profile. Ekelund et al. (24) found that physical activity and cardiorespiratory fitness are separately and independently associated with individual and clustered metabolic risk factors in children and suggested that physical fitness and activity affect metabolic risk through different pathways. Recently, Schindler et al. (25) concluded that there are close relationships between physical activity and cardiorespiratory fitness parameters in children. However, there is no information available how high aerobic fitness level is genetically related to metabolic syndrome markers during pubertal development.

Growth and metabolic syndrome

Growth spurt varies considerably in timing, rate and duration among individuals. Allowing for variation, peak height velocity rather than chronological age has been used to characterize changes in size, body composition and performance relative to adolescent spurt in height (11). For example, from about 13-14 years of age, boys advanced in maturity status (sexual and skeletal maturation) are better represented in youth soccer teams (26). Regular physical exercise has no effect on the rate of growth in height and on the adult stature as revealed by different longitudinal studies (27,28). However, it is still not clear whether there is a specific critical period during the growing years when bones may be most responsible to exercise (29). Regular exercise is also associated with higher aerobic fitness level during childhood and adolescence (30,31), but particularly after puberty (32). In contrast, sedentary children and adolescents have been shown to have lower cardiorespiratory fitness level (11). However, how this relatively low cardiorespiratory fitness level exactly influences most of the metabolic syndrome parameters is still unknown.

Exercise does not affect skeletal maturity in boys (33), and age at peak height velocity is not influenced by the level of habitual physical activity (11). Fitness, fatness and metabolic syndrome have been studied together in children and adolescents (18,34). In Spanish adolescence, high cardiorespiratory fitness correlated with age-and sex-specific standardized values of triglycerides, LDL-s, HDL-s and fasting glucose (35). Ruiz et al. (36) concluded that boys with peak oxygen consumption ($\dot{V}O_2$peak/kg) above 42.1 ml/min/kg were 2.42 times more likely to have a low metabolic risk when compared with those with $\dot{V}O_2$max/kg levels below this value. Recently Steele et al. (37) concluded that both physical activity and cardiorespiratory fitness are separately and independently associated with metabolic risk factors in youth, possibly through different casual pathways. Low levels of physical activity and aerobic fitness in childhood have been associated with the presence of the metabolic syndrome in adolescence (38). The results of Ventura et al. (39) suggest that neither physical activity nor inactivity during childhood is related to metabolic syndrome but aerobic fitness (measured by the 20 m shuttle run) is correlated significantly with metabolic syndrome. In children and adolescents cardiovascular fitness is inversely associated with abdominal adiposity (40). Longitudinal investigations will help disclose possible long-term relationships of physical activity patterns and cardiorespiratory fitness achieved in early childhood with metabolic risk factors later on in life.

Genetics and metabolic syndrome

Several studies support the hypothesis that there are significant genetic components to variation in endurance performance in untrained state. The heritability of $\dot{V}O_2$peak is about 50% (41) or accounting for 25-60% of the total phenotype variability (42). In the most recent version of the human gene map for physical performance and health-related fitness, 18 autosomal and 3 mitochondrial genes were associated with endurance phenotypes (43). Two genes have received more attention: angiotensin converting enzyme (ACE) and ά-actinin 3 (ACTN3). Since the first report in 1997, 42 publications have reported results from association studies on exercise-related phenotypes with an insertion deletion variant in the ACE locus. The I allele, which is associated with lower circulating ACE activity, has been reported to be more frequent in endurance athletes than in sedentary controls and to be associated with higher aerobic capacity. Contrary, some studies have reported that D allele (associated with high circulating ACE levels) is associated with better performance in short-duration sprints and in strength-related tasks. However, the results are inconclusive due to numerous negative studies and by the almost universal lack of statistical power (11). Moran et al. (44) found that the ACE gene haplotypes (including rs4424958 and rs4311) did not explain no significantly greater proportion of the phenotypic variance than I/D polymorphism analyzed alone. This may suggest that the majority of the genetic effects are accounted for either by the I/D polymorphism or a variant in strong linkage disequilibrium with it. ACE gene I/D polymorphism shows stronger association with the levels of circulating ACE activity in Caucasians than do other ACE variants (45). Studies on genetics on physical activity level are not extensive, but evidence from both twin and family studies suggests that genetic factors could be involved in the determination of physical activity level. Moreover, there is very limited data in the literature on genetic predisposition to physical activity. Some of the candidate genes like dopamine D2 receptor, leptin receptor, melanocortin 4 receptor were investigated with an a priori hypothesis on the association between physical activity and DNA sequence variation (46-48). Research has not shown yet whether there is genetic predisposition to habitual physical activity level. It is also important to recognize that being physically active is not necessarily the same as being engaged in exercise training. Physically active children, who are involved in exercise training groups might exercise because of their parents´ will. For example is a child carrying the I allele of the ACE gene more physically active due to higher aerobic capacity?

Adipocytokines and metabolic risk factors

Research into the mechanisms and mediators of obesity-related sequences has greatly expanded over the last years and, in this respect, factors released from adipose tissue appear to be particularly important. Adipose tissue is currently thought to be not only a depot for energy storage but has now been considered as an endocrine organ that produces many molecules having biological activity, called adipocytokines. Among the adipocytokines, leptin was the first adipocytokine detected and studied (49). Leptin is a hormone that is primarily synthesized and produced by adipocytes and it is identified as a key factor in maintaining energy balance and overall body composition. Leptin concentration has been documented to positively correlate with percent body fat in children. More specifically, leptin has been found to have a positive relationship with BMI and fat mass, a negative correlation to fat-free mass and is usually higher in obese children relative to lean children (50). Leptin levels also correlate closely with insulin resistance indices (HOMA-IR) and blood lipids (51). Adiponectin is one of the most abundant circulating adipose tissue-specific adipocytokines. Adiponectin is produced in visceral, subcutaneous and bone marrow fat depots (52). In contrast to other adipocytokines, adiponectin expression is negatively

regulated in obesity and decreased levels are associated with parameters of the metabolic syndrome in adults (32,52). Böttner et al. (53) found that there was a decline in adiponectin levels with the progression of puberty and that decline was inversely related to testosterone concentration in boys. Adiponectin concentration is inversely correlated with insulin, triglycerides and very low density lipoprotein levels and positively correlated with HDL levels (54). Körner et al. (51) concluded that adiponectin is obviously a very early predictor of metabolic syndrome in children. Gilardini et al. (55) showed that adiponectin was the only factor that correlated with all the components of the metabolic syndrome in obese children and adolescents. In 10-14 year olds Rubin et al. (56) found that from the anthropometrical parameters waist circumference and subscapular and triceps skinfolds seem to be more closely associated with selected cytokines (TNF-alpha, IL-6, resistin and adiponectin) than a BMI percentile indicating obesity. Adiponectin plays an important role in the control of metabolic dysfunction and restoration to normal levels may potentially contribute to better health outcomes by improving glucose homeostasis, insulin sensitivity and fatty acid oxidation in adults (57). However, to date the youngest subjects in the studies that have investigated the influence of physical activity and exercise on adiponectin concentration have been 13 year old obese adolescents (57). Accordingly, there are no studies that have longitudinally investigated the possible role of adiponectin in the development of metabolic risk factors in children throughout puberty.

Increases in adiponectin levels with weight loss were significantly associated with the improvements in insulin sensitivity, suggesting that adiponectin may be one of the key molecules in the determination of the metabolic syndrome and its risk factors (54). A number of adiponectin gene (ADIPOQ) single nucleotide polymorphisms (SNP) have been associated with plasma adiponectin levels, however with controversial results. A synonymous SNP in exon 2 (45 G>T) has been inconsistently reported to be associated with type 2 diabetes (58,59). Another SNP in intron 2 (276 G>T) has been associated with IR as assessed by HOMA-IR and reduced levels of adiponectin in Japanese (59). Shin et al (60) showed that changes in plasma adiponectin concentration were inversely correlated with changes in HOMA-IR after mild weight loss in obese Korean subjects. The GG homozygotes had significantly higher degrees of IR than carriers of the T allele at ADIPOQ 276 T>G and there was a different adiponectin response between GG homozygotes and T allele carriers after weight loss (60). Thus, the genetic components of the ADIPOQ gene that result in different adiponectin concentration in blood may be partly responsible for the pathogenesis of the metabolic risk factors. However, those studies mostly involve normal and/or overweight adults with much less data on pubertal children. It is not clear whether the genotype effect on adiponectin is already present during puberty or it rather develops during adulthood. Furthermore, if a weight loss might have different adiponectin response on subjects with different genotype, could the differences in physical activity (i.e. high vs low) lead to similar findings, or the negative energy expenditure during weight loss would be the key factor. Our previous results in adults suggest that physical activity may have an influence on adiponectin concentration (32).

Conclusions

Several metabolic risk factors have been presented. It is well established that both physical activity and physical fitness highly influence all metabolic risk factors. However, as a rule there is almost no longitudinal studies, especially during puberty when the children grow rapidly. It is unknown, whether genetically high aerobic capacity in children have lower risk to metabolic syndrome risk factors. What should be the minimal level of physical activity recommended that they need. Probably the physical activity level is more important at the later stages of pubertal development and physical activity level is not dependent on genetic predisposition during pubertal development.

Adipocytokines correlate highly with most of metabolic syndrome risk factors. Very promising is adiponectin. However, hypothetically genetic polymorphism in adiponectin gene do not influence fasting concentration of adiponectin independent of body composition and physical activity level.

References

1. Teran-Garcia M, Rankinen T, Bouchard C. Genes, exercise, growth, and the sedentary, obese child. *J Appl Physiol* 2008; 105: 988-1001.
2. Raitakari OT, Juonala M, Kahonen M, et al. Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study. *JAMA* 2003; 209: 2277-83.
3. Pietrobelli A, Malavolti M, Battistini NC, et al. Metabolic syndrome: a child is not a small adult. *Int J Pediatr Obes* 2008; 3 (Suppl.): 67-71.
4. Zimmet P, Alberti KG, Kaufman E, et al. The metabolic syndrome in children and adolescence – an IDF consensus report. *Pediatr Diab* 2007; 8: 299-306.
5. Zimmet P, Alberti G, Kaufman E, et al. The metabolic syndrome in children and adolescence. *Lancet* 2007; 369: 2059-61.
6. Reaven GM. The metabolic syndrome: is this diagnosis necessary? *Am J Clin Nutr* 2006; 83: 1237-47.
7. Kwiterovich PO. Clinical and laboratory assessment of cardiovascular risk in children: guidelines for screening, evaluation, and treatment. *J Clin Lipidology* 2008; 2: 248-66.
8. Andresen LB, Harro M, Sardinha LB, et al. Physical activity and clustered cardiovascular risk in children: a cross-sectional study. (The European Youth Heart Study). *Lancet* 2006; 368: 299-304.

9. Cruz ML, Goran MI. The metabolic syndrome in children and adolescence. *Curr Diab Rep* 2004; 4: 53-62.
10. Spalding KL, Arner E, Westermark PO, et al. Dynamics of fat cell turnover in humans. *Nature* 2008; 453: 783-7.
11. Malina RM, Bouchard C, Bar-Or O. Growth, maturation, and physical activity. Champaign, IL: Human Kinetics, 2004.
12. Baumgartner RN, Roche AF, Guo S, et al. Adipose tissue distribution – the stability of principal components by sex, etnics, and maturation stage. *Hum Biol* 1986; 58: 719-35.
13. Caspersen CJ, Powell EK, Christenson GM. Physical activity, exercise and physical fitness: definitions and distinctions for health-related research. *Publ Hlth Rep* 1985; 100: 126-31.
14. Trost SG. Objective measurement of physical activity in youth: current issues, future directions. *Exerc Sport Sci Rev* 2001; 29: 32-6.
15. Corder K, Ekelund U, Steele M, et al. Assessment of physical activity in youth. *J Appl Physiol* 2008; 105: 977-87.
16. van Mechelen W, Twisk JW, Post GB, et al. Physical activity of young people: the Amsterdam Longitudinal Growth and Health Study. *Med Sci Sports Exerc* 2000; 32: 1610-6.
17. Yang X, Telama R, Hirvensalo M, et al. The longitudinal effects of physical activity history on metabolic syndrome. *Med Sci Sports Exerc* 2008; 40: 1424-31.
18. Twisk JW. Physical activity, physical fitness and cardiovascular health. In: Armstrong N, van Mechelen W., ed. Pediatric Exercise and Medicine. Oxford: Oxford University Press, 2000, p. 253-63.
19. Platat C, Wagner T, Klumpp T, et al. Relationships of physical activity with metabolic syndrome features and low-grade inflammation in adolescents. *Diabetologia* 2006; 49: 2078-85.
20. Pan Y, Pratt CA. Metabolic syndrome and its association with diet and physical activity in US adolescents. *J Am Diet Assoc* 2008; 108: 276-86.
21. Leary SD, Ness AR, Smith GD. Physical activity and blood pressure in childhood: findings from a population based study. *Hypertension* 2008; 51: 92-8.
22. Bouchard C, Shephard RJ. Physical activity, fitness, and health: the model and key concepts. In: Bouchard C., Shephard R.J., Stephens T. ed. Physical activity, fitness, and health: international proceedings and consensus statement. Champaign, IL: Human Kinetics, 1994, p. 77-88.
23. Rizzo NS, Ruiz JR, Hurtig-Wennlof A, et al. Relationship of physical activity, fitness and fatness with clustered metabolic risk in children and adolescents: the European Youth Heart Study. *J Pediatr* 2007; 150: 388-94.
24. Ekelund U, Anderssen SA, Froberg G. Independent associations of physical activity and cardiorespiratory fitness with metabolic risk factors in children: the European Youth Heart Study. *Diabetologia* 2007; 50: 1832-40.
25. Shindler C, Siegert J, Kirch W. Physical activity and cardiovascular performance – how important is cardiorespiratory fitness in childhood? *J Publ Hlth* 2008; 16: 235-43.
26. Philippaerts RM, Vaeyens R, Janssens M, et al. The relationship between peak height velocity and physical performance in youth soccer players. *J Sports Sci* 2006; 24: 221-30.
27. Beunen GP, Malina RM, Renson R, et al. Physical activity and growth, maturation and performance: a longitudinal study. *Med Sci Sports Exerc* 1992; 24: 576-85.
28. Saris WHM, Elvers JWH, Van´t Hof MA, et al. Change in physical activity of children aged 6 to 12 years. In: Rutenfranz J, Mocellin R, Klimpt F., ed. Children and Exercise XII. Champaign, IL: Human Kinetics, 1986, p. 121-30.
29. Daly R. The effect of exercise on bone mass and structural geometry during growth. In: Daly R., Petit M., ed. Optimizing Bone Mass and Strength. The Role of Physical Activity and Nutrition During Growth. Basel: Karger, 2007, p. 33-49.
30. Kemper HC, Twisk JW, Koppes LL., et al. A 15 year physical activity pattern is positively related to aerobic fitness in young males and females (13-27 years). *Eur J Appl Physiol* 2001; 84: 395-402.
31. Mirwald RI, Bailey DA. Maximal Aerobic Power. London, Ontario: Sport Dynamics, 1986.
32. Jürimäe J, Jürimäe T. Plasma adiponectin concentration in healthy pre- and postmenopausal women: relationship with body composition, bone mineral, and metabolic variables. *Am J Physiol Endocrinol Metab* 2007; 293: E42-7.
33. Beunen G, Thomis M. Genetic determinants of sport participation and daily physical activity. *Int J Obes* 1999; 23 (suppl. 3): 555-63.
34. Goran WI. Energy expenditure, body composition, and disease risk in children and adolescence. *Prog Nutr Soc* 1997; 56: 195-209.
35. Mesa JI, Ortega FB, Ruiz JR, et al. The importance of cardiorespiratory fitness for healthy metabolic traits in children and adolescents: the Avena Study. *J Publ Hlth* 2006; 14: 178-80.
36. Ruiz JR, Ortega FB, Rizzo NS, et al. High cardiovascular fitness is associated with low metabolic risk score in children: The European Youth Heart Study. *Ped Res* 2007; 61: 350-5.
37. Steele RM, Brage S, Corder K, et al. Physical activity, cardiorespiratory fitness, and the metabolic syndrome in youth. *J Appl Physiol* 2008; 105: 342-51.
38. McMurray RG, Bangdiwala SI, Harrell JS, et al. Adolescence with metabolic syndrome have a history of low aerobic fitness and physical activity levels. *Biodyn Led* 2008; 7: 1-6.
39. Ventura AK, Loken E, Birch LL. Risk profiles for metabolic syndrome in a non clinical sample of adolescence girls. *Pediatr* 2006; 118: 2434-42.
40. Ortega FB, Ruiz JR, Hurtig-Wennlöf A, et al. Cardiovascular fitness modifies the associations between physical activity and abdominal obesity in children and adolescence. The European Youth Heart Study. *Br J Sports Med* 2008. In Press.
41. Bouchard C, Daw EW, Rice T, et al. Familial resemblance for VO_2max in the sedentary state: The Heritage Family Study. *Med Sci Sports Exerc* 1998; 30: 252-8.
42. Bouchard C, Dionne FT, Simoneau J-A, et al. Genetics of aerobic and anaerobic performance. *Exerc Sport Sci Rev* 1992; 20: 27-58.
43. Rankinen T, Bray MS, Hagberg JM, et al. The human gene map for performance and health-related fitness phenotypes: the 2005 update. *Med Sci Sports Exerc* 2006; 38: 1863-88.
44. Moran CN, Vassipolopoulus C, Tsiokanos A, et al. The association of ACE polymorphisms with physical, physiological and skill parameters in adolescents. *Eur J Hum Gen* 2006; 14: 332-9.
45. Soubrier F, Martin S, Alonso A, et al. High-resolution genetic mapping of the ACE-linked QTL influencing circulating ACE activity. *Eur J Hum Genet* 2002; 10: 553-61.
46. Loos RJ, Rankinen T, Tremblay A, et al. Melanocortin-4 receptor gene polymorphism, circulationg calcium concentrations and bone mineral density in the Quebec Family Study. *Int J Obes* 2005; 29: 420-8.
47. Simonen RI, Rankinen T, Perusse L, et al. A dopamine D2 receptor gene polymorphism and physical activity in two family studies. *Physiol Behav* 2003; 78: 751-7.
48. Stefan N, Vozarova B, Del Parigi A, et al. The Gln223Arg polymorphism of the leptin receptor in Pima Indians: influence on energy expenditure, physical activity and lipid metabolism. *Int J Obes Relat Metab Disord* 2002; 26: 1629-32.
49. Zhang Y, Proenca R, Maffei M, et al. Positional cloning of the mouse obese gene and its human homologue. *Nature* 1994; 372: 425-32.
50. Venner AA, Lyon ME, Douyle-Baker PK. Leptin: a potential biomarker for childhood obesity? *Clin Biochem* 2006; 39: 1047-56.
51. Körner A, Kratzsch J, Gausche R, et al. New predictors of the metabolic syndrome in children – role of adipocytokines. *Ped Res* 2007; 61: 640-65.
52. Koemer A, Kratzsch J, Kiess W. Adipocytokines: leptin – the classical, resistin – the controversial, adiponectin – the promising, and more to come. *Best Pract Res Clin Endocrinol Metab* 2005; 19: 525-46.
53. Böttner A, Kratzsch J, Müller G, et al. Gender differences of adiponectin levels develop during the progression of puberty and are related to serum androgen levels. *J Clin Endocrinol Metab* 2004; 89: 4053-61.

54. Bacha F, Saad R, Gungor R, et al. Adiponectin in youth. Relationship to visceral adiposity, insulin sensitivity and ß-cell function. *Diab Care* 2004; 27: 547-52.
55. Gilardini L, McTernan PG, Girola A, et al. Adiponectin is a candidate marker of metabolic syndrome in obese children and adolescence. *Atherosclerosis* 2006; 189: 401-7.
56. Rubin DA, McMurray RG, Harrell JS, et al. Do surrogate markers for adiposity relate to cytokines in adolescence? *J Investig Med* 2008; 56: 786-92.
57. Simpson KA, Singh AF. Effects of exercise on adiponectin: a systematic review. *Obesity* 2008; 16: 241-56.
58. Vasseur F, Helbecque N, Dina C, et al. Single-nucleotide polymorphism haplotypes in the both proximal promoter and exon 3 of the apm1 gene modulate adipocyte-secreted adiponectin hormone levels and contribute to the genetic risk for type 2 diabetes in French Caucasians. *Hum Mol Genet* 2002; 11: 2607-14.
59. Hara K, Boutin P, Mori Y, et al. Genetic variation in the gene encoding adiponectin is associated with an increased risk of type 2 diabetes in the Japanese population. *Diabetes* 2002; 51: 536-40.
60. Shin MJ, Yang Y, Koh SJ, et al. The association of SNP276G>T at adiponectin gene with circulating adiponectin and insulin resistance in response to mild weight loss. *Int J Obes* 2006; 30: 1702-8.

Received: November 10, 2008
Accepted: February 05, 2009
Published: February 10, 2009

Address for correspondence:
Prof. Toivo Jürimäe PhD
Institute of Sport Pedagogy and Coaching Sciences
Faculty of Exercise and Sport Sciences
University of Tartu
18 Ülikooli Street
50090 Tartu
Estonia
Phone: +372-7-375 372
Fax: +372-7-375 373
E-mail: toivo.jurimae@ut.ee

Jaak Jürimäe: jaak.jurimae@ut.ee
Jarek Mäestu: jarek.maestu@ut.ee