

# Sedentarism and Physical Inactivity Patterns Correlated with HOMA-IR in European Adolescents, the Helena Study

Kondakis Makra Aikaterini<sup>1\*</sup>, Katerina Kondaki<sup>1</sup>, Georgia Kurlaba<sup>1</sup>, Evangelia Grammatikaki<sup>1</sup>, Yannis Manios<sup>1</sup>, David Jiménez Pavón<sup>2</sup>, Stefaan De Henauw<sup>3</sup>, Marcela González-Gross<sup>4</sup>, Michael Sjöström<sup>5</sup>, Frédéric Gottrand<sup>6</sup>, Dénes Molnar<sup>7</sup>, Luis A Moreno<sup>8</sup>, Anthony Kafatos<sup>9</sup>, Chantal Gilbert<sup>10</sup> and Mathilde Kersting<sup>11</sup>

<sup>1</sup>Department of Nutrition and Dietetics, Harokopio University, Athens, Greece

<sup>2</sup>Department of Physiology, School of Medicine, University of Granada, Granada, Spain

<sup>3</sup>Department of Public Health, Ghent University, Ghent, Belgium

<sup>4</sup>Department of Health and Human Performance, Facultad de Ciencias de la Actividad Física y del Deporte, Universidad Politécnica de Madrid, Madrid, Spain

<sup>5</sup>Karolinska Institutet (Sweden)

<sup>6</sup>Faculté de médecine, University of Lille 2, Lille, France

<sup>7</sup>Department of Pediatrics, University of Pécs, Pécs, Hungary

<sup>8</sup>Escuela Universitaria de Ciencias de la Salud, Universidad de Zaragoza, Zaragoza, Spain

<sup>9</sup>Preventive Medicine and Nutrition Unit, University of Crete School of Medicine, Heraklion, Crete, Greece

<sup>10</sup>Campden BRI (United Kingdom)

<sup>11</sup>Research Institute of Child Nutrition Dortmund, Rheinische Friedrich-Wilhelms-Universität Bonn (Germany)

## Abstract

**Objective:** The aim of the present study was to examine the independent association between time spent on sedentary activity, either objectively measured or self-reported and IR proxy measures in European adolescents.

**Methods:** A subset (n=1,097) of a large multicentre European study in adolescents (HELENA-CSS study) was used in the present study. Homeostasis model assessment (HOMA)-IR was calculated. Serum concentrations of glucose (GF) and insulin (IF) were measured after an overnight fast. The HOMA-IR was calculated as  $IF (\mu IU/mL) \times GF (mmol/l)/22.5$  (to convert IF values in  $\mu IU/mL$  to  $pmol/l$  multiply by 6.945) sedentary time and the time spent on moderate-to-vigorous physical activity (MVPA) was objectively measured by using accelerometers. Moreover, the daily minutes spent on sedentary activities were recorded through a self-report sedentary behaviour questionnaire.

**Results:** Univariate analyses showed that HOMA-IR levels were significantly higher among adolescents watching TV  $\geq 2$ h/day (1.87 (C.I.1.31, 2.66)) compared to the rest of adolescents (2.02 (1.44, 2.82),  $p=0.011$ ). Moreover, the objectively measured MVPA was inversely correlated to HOMA-IR ( $\rho=-0.117$ ,  $p=0.023$ ). Multilevel linear regression analysis revealed that adolescents watching TV  $\geq 2$  h/day had significantly higher HOMA-IR even after controlling for gender, age, total energy intake, total fat intake, simple carbohydrate intake and pubertal stage ( $p=0.007$ ). Further adjustment for MVPA, showed that TV viewing time remained significantly related to the IR ( $p=0.002$ ). In this model, MVPA was also inversely associated with HOMA-IR levels ( $p=0.001$ ). Finally, further controlling for waist circumference showed that adolescents exceeding the limit of 2 h/day watching TV continued to have higher HOMA-IR levels ( $p=0.002$ ). Stratified analysis by BMI status, revealed that TV viewing time is independently associated with HOMA-IR only among normal weight adolescents, while MVPA was inversely associated with IR in both overweight/obese and normal weight adolescents.

**Conclusions:** The results of the present study indicate that time spent watching TV and at MVPA is related to IR independent of central fat mass and total energy intake in normal weight European adolescents, while MVPA seems to protect adolescents from developing IR even among overweight/obese adolescents. Therefore, intervention programmes aiming at reducing sedentary behaviours and increasing overall moderate-intensity activities should be implemented.

## Introduction

The prevalence of Insulin Resistance (IR) in children and adolescents is increasing in both developing and industrialized countries [1-5]. Although, there is no universally accepted definition of IR, all studies aiming to estimate the prevalence of IR indicate that more than one third of obese children or adolescents display IR, while an almost 3% IR prevalence has been detected among normal weight children [2,4,5].

IR, considered a major characteristic of the metabolic syndrome, is a precursor of type 2 diabetes and it has been associated with cardiovascular disease and metabolic disorders such as hypertension, dyslipidemia, hepatic steatosis, endothelial dysfunction [6,7]. Several modifiable and non-modifiable risk factors such as genotype, age, overall and abdominal obesity, dietary factors, physical activity (PA) have been identified for IR [7-12]. In particular, the inverse correlation of PA with various markers of IR among children and adolescents has been extensively evaluated [13-19]. However, the main body of existing

research has been conducted among overweight and obese children/adolescents [17-19]. Moreover, limited data are available regarding the independent associations between different subcomponents of PA

\*Corresponding author: Kondakis Makra Aikaterini, Department of Nutrition and Dietetics, Harokopio University, Athens, Greece, Tel: 00306947202356; Fax: 00302130222789; E-mail: [kondakikaterina@live.com](mailto:kondakikaterina@live.com)

Received September 26, 2017; Accepted October 12, 2017; Published October 20, 2017

Citation: Aikaterini KM, Kondaki K, Kurlaba G, Grammatikaki E, Manios Y, et al. (2017) Sedentarism and Physical Inactivity Patterns Correlated with HOMA-IR in European Adolescents, the Helena Study. J Nutr Food Sci 7: 638. doi: 10.4172/2155-9600.1000638

Copyright: © 2017 Aikaterini KM, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

(i.e. time spent sedentary, at light-intensity activity and at moderate- and vigorous intensity physical activity (MVPA) and self-reported TV viewing) and IR, especially among children/adolescents [13,20,21].

Sedentary behaviour, defined as self-reported TV viewing or total sitting time, has been associated with abnormal glucose metabolism [22,23] and the metabolic syndrome [24] as well as predicts obesity and type 2 diabetes in adults [25]. Moreover, a recently published study conducted among adults showed that objectively measured sedentary time predicts higher levels of fasting insulin independent of the amount of time spent at MVPA [20]. To the best of our knowledge, just a few in this field has been conducted aiming to elucidate the association between time spent active and IR among children and revealed the importance of decreasing sedentary behaviour. For instance the European Youth Heart Study (EYHS) concluded that Physical activity is inversely associated with fasting insulin in the non-diabetic range of fasting glucose. The relationship was stronger for insulin than for glucose, indicating compensatory action by the beta cells. Our data emphasise the importance of physical activity in children for the maintenance of metabolic control and increasing time spent in moderate- and vigorous-intensity activity in adolescents may have beneficial effects on metabolic risk factors regardless of the degree of adiposity [13].

This finding is important because existing guidelines on PA for public health emphasize the importance of MVPA but do not consider the potential harmful effects of sedentary living. The average amount of daily sedentary time in European adolescents has previously objectively measured through the Healthy Lifestyle in Europe by Nutrition in Adolescents Cross-Sectional Study (HELENA-CSS), a multicentre, cross-sectional study performed in 9 European countries [25,26]. This study revealed that adolescents spent most of their time in sedentary behaviours. However, to the best of our knowledge, data regarding the association between sedentary life and IR in European adolescents are few and unjustified. Therefore, the aim of the present study was to examine the independent association between time spent sedentary, either objectively measured or self-reported and IR proxy measures in European adolescents.

## Material and Methods

### Research design

The HELENA-CSS was carried out in 10 European cities: Athens (Greece), Dortmund (Germany), Ghent (Belgium), Heraklion (Greece), Lille (France), Pécs (Hungary), Rome (Italy), Stockholm (Sweden), Vienna (Austria) and Zaragoza (Spain) [25]. A total of 3,865 adolescents aged 12.5 yrs to 17.5 yrs were recruited at high schools and met the general HELENA-CSS inclusion criteria: not participating simultaneously in another clinical trial and be free of any acute infection lasting less than 1 week before the inclusion and having information on weight and height. Data collection from the HELENA-CSS took place in 2006 and 2007. More details are presented elsewhere [25].

In the current study a total of 1,097 adolescents (583 females and 514 males) with complete data on glucose and insulin levels but around 700 with data from accelerometers were included. Ethics committees from each country approved the HELENA-CSS protocols [26].

### Anthropometric measurements

Weight was measured in underwear and without shoes with an electronic scale (Type SECA 861) to the nearest 0.05 kg and height was measured barefoot in the Frankfurt plane with a telescopic height

measuring instrument (Type SECA 225) to the nearest 0.1 cm. BMI was calculated as body weight (kg) divided by the height squared (m<sup>2</sup>) [27]. Age- and sex-standardized BMI cut-off points according to the International Obesity Task Force were used to define normal-weight, overweight and obesity [28]. Waist circumference (WC) was measured in triplicate at the midpoint between the lowest rib and the iliac crest with an anthropometric tape SECA 200 [29] and was used as a surrogate of central body fat. Standard instructions for BIA measurements were followed. Pubertal stage was recorded by a researcher of the same sex as the child, after brief observation according to Tanner and Whitehouse [30,31].

### Physical activity assessment

PA was measured by using accelerometers (Actigraph MTI, model GT1M, Manufacturing Technology Inc., Fort Walton Beach, FL, USA) placed on each individual for seven days. More details regarding PA assessment can be found in Hagstromer et al. The following variables were derived: the time (min/day) spent in sedentary activities (<500 counts/min) and at light PA (500 to 1999 counts/min), moderate PA (2000 to 3999 counts/min) and vigorous PA ( $\geq$  4000 counts/min). The MVPA stands for the time spent on at least 2000 counts/min.

### Self-reported sedentary behavior

A self-report sedentary behavior questionnaire (designed ad hoc) was administered during the school hours as described elsewhere [32]. Adolescents reported the daily minutes spent on the following sedentary items: TV viewing, playing with computer games and console games, surfing by internet for reasons other than study, for week and weekends days. Thereinafter, taking into account the recommendations of the American Academy of Pediatrics (AAP) regarding children's TV watching time, the participants were divided into two groups as follows: children watching TV less than 2 h/day and those watching TV 2 h/day and more [33]. Moreover, the total self-reported sedentary time was calculated by summing the time spent on TV viewing, playing with computer and console games and surfing on internet.

### Dietary assessment

Population mean for intakes and distributions for participants in different European countries were collected with the 24-h recall method. Furthermore, usual intake was estimated by statistical modelling techniques using two non-consecutive 24-h recalls [34]. Following these recommendations and regarding the challenges to measure food consumption in adolescents, a computer-assisted self-administered tool (HELENA-DIAT, previously known as YANA-C), attractive for adolescents, was adapted for dietary assessment in the HELENA CSS [34,35]. To calculate energy and nutrient intakes, food intake information were linked to local food composition databases (FCDBs) [36].

### Blood samples

Serum concentrations of glucose (GF) and insulin (IF) were measured after an overnight fast. The HOMA-IR was calculated as  $IF (\mu\text{U/mL}) \times GF (\text{mmol/l}) / 22.5$  (to convert IF values in  $\mu\text{U/mL}$  to pmol/l multiply by 6.945) [37]. A detailed description of the blood analysis has been reported elsewhere [37,38].

### Statistical analysis

Normally distributed continuous variables are expressed as mean values  $\pm$  standard deviation and skewed variables are reported as median (25th, 75th percentiles). Normality of distribution was evaluated through the Kolmogorov-Smirnov test. HOMA-IR was

not normally distributed and then log-transformed values were used. Categorical variables are summarized as relative frequencies (%). Associations between categorical variables were tested by using the Chi-Square test. The associations between the continuous and binary variables (i.e., gender) were evaluated through Student's t-test or Mann-Whitney when the former were normally or skewed distributed, respectively. Correlations between subcomponents of PA and HOMA-IR were tested by the use of Spearman correlation.

Multilevel linear regression analyses were performed with adolescents nested within classes nested within schools (three-level random intercept model) in order to assess the associations between PA subcomponents (independent variables) and HOMA-IR levels (dependent variable). Three different models were performed for each PA subcomponent, separately. In the Model 1 the association of each PA subcomponent with HOMA-IR was evaluated after adjusting for gender, age, total energy intake, total fat intake, simple carbohydrate intake and the pubertal stage. In the Model 2, MVPA was further included as a potential confounder and in the Model 3 the WC, as indicator of central obesity, was further entered in the model. In the Model 3, the interaction term between gender and PA component was used in order to elucidate whether gender modifies the association between PA subcomponent and HOMA-IR. The results are presented as  $\beta$ -coefficients and 95% confidence interval (95% CI). P-values < 0.05 from two-sided hypotheses are considered as statistically significant. The SPSS 18.0 (SPSS Inc., Texas, USA) statistical software was used to conduct all statistical analyses.

## Results

Table 1 shows descriptive characteristics of the sample. As concerns PA subcomponents, it was found that the daily time spent playing computer and/or console games, as well as the time spent on MVPA was statistically significantly higher among boys compared to girls, while no difference was detected on TV viewing time, time spending on surfing by internet and at objectively measured sedentary activities (Table 1). Moreover, the TV viewing time was equal to or more than 2 h/day in 38.8% of adolescents. The percentage of boys exceeding the limit of 2 h/day was statistically significantly higher (42.4%) compared to girls (35.7%,  $p=0.023$ ).

With respect to IR indicators, both IF levels and HOMA-IR levels were significantly higher in girls compared to boys (Table 1).

Univariate correlation coefficients between PA subcomponents and HOMA-IR are presented in Table 2 for the total sample, by gender and for underweight/normal weight and overweight/obese, separately. Among the self-reported sedentary activities, TV viewing time was found to be positively, significantly associated with HOMA-IR in the total sample, both genders and normal weight adolescents (Table 2). Moreover, HOMA-IR levels were found to be statistically significantly higher among adolescents watching TV at least 2 h/day (1.87 (1.31, 2.66)) compared to the rest of adolescents (2.02 (1.44, 2.82),  $p=0.011$ ). In addition to TV viewing time, the time spending on playing computer and/or console games was found to be positively related to HOMA-IR both in boys and girls when stratified analysis by gender was

Parameters	Total	Males	Females
	N=1089	N= 580	N=509
<b>Age (years) §</b>	14.83 ± 1.2	14.76±1.2	14.70 ±1.1
<b>Anthropometric measures§</b>			
BMI (kg/m <sup>2</sup> )	21.4 ± 3.7	21.4 ± 4.0	21.3 ± 3.3
Waist circumference (cm)	72.4 ± 8.6	74.4 ± 9	70.7 ± 7.8*
<b>Tanner stage‡</b>			
1	0.70%	1.60%	0.6%*
2	6.20%	8.10%	5.50%
3	20.90%	20.10%	18.50%
4	42.90%	41.60%	38.10%
5	29.30%	28.60%	26.10%
<b>Self-reported sedentary time (min/day)</b>			
TV viewing †	107 (58, 167)	107 (70, 167)	107 (58, 167)
Playing on computer and console games †	56 (9, 124)	105 (39, 183)	24 (0, 75)*
Surfing by Internet †	45 (11, 91)	45 (11, 90)	45 (11, 107)
Total sedentary time (min/day)†	227 (141, 349)	272 (180, 399)	193 (120, 298)*
<b>Objectively measured PA</b>			
Time spent inactive (<100counts/min)§	543 ± 86	535.96 ± 93	547.79 ± 78
Time spent on MVPA (>2000counts/min) §	59 ± 24	69.24 ± 25.11	51.07 ± 20.30*
<b>Biochemical measurements</b>			
Insulin (µIU/mL)†	8.65 (6.20, 12.0)	8.17 (5.93, 11.50)	9.12 (6.57, 12.30)*
HOMA-IR†	1.95 (1.37, 2.72)	1.87 (1.33, 2.69)	2.04 (1.39, 2.77)*
<b>Energy and macronutrients intake</b>			
<b>Total energy (kcal/day) §</b>	2261 ± 1018	2646 ± 1134	1928 ± 763*
<b>Total carbohydrate (gr./day) §</b>	273 ± 129	318 ± 149	233 ± 91*
<b>Total fat(gr./day)§</b>	91 ± 50	106 ± 56	77 ± 40*

§ Data are presented as mean ± sd  
† Data are presented as median (interquartile range)  
‡ Data are presented as percentages  
\* p-value < 0.05 between boys and girls

Table 1: Baseline characteristics of population.

conducted, while no correlation was detected when stratified analysis by BMI status was carried out. Furthermore, the total self-reported sedentary time was found to be significantly correlated with IR in the overall sample, while when stratified analyses by gender and BMI status were performed, the significant correlation was detected only among girls and normal weight adolescents. Finally, among the objectively measured PA subcomponents, only the MVPA was significantly inversely correlated to HOMA-IR (Table 2).

Multilevel multiple linear regression revealed that adolescents watching TV  $\geq 2$  h/day had statistically significantly higher HOMA-IR levels even after controlling for gender, age, total energy intake, total fat intake, simple carbohydrate intake and pubertal stage ( $p=0.007$ , Model 1) (Table 3). Similar results were detected even treating TV viewing time as a continuous variable (data not presented). Further adjustment for MVPA, showed that TV viewing time remained significantly related to the IR ( $p=0.002$ , Model 2) (Table 3). In this model, MVPA was also inversely associated with HOMA-IR levels ( $p=0.001$ ). Finally, further adjustment for WC although attenuated the association between TV viewing time and HOMA-IR levels, the adolescents watching TV  $\geq 2$  h/day continued to have higher HOMA-IR levels ( $p=0.002$ , Model 3) (Table 3). This association was not found to be modified by the gender ( $p$  for interaction between TV viewing time and gender= $0.731$ ). Stratified analysis by BMI status, revealed that TV viewing time is independently associated with HOMA-IR only among normal weight

adolescents (Tables 4a and 4b). However, MVPA was found to be significantly and inversely associated with IR in both overweight/obese and normal weight adolescents (Tables 4a and 4b).

Substituting in the aforementioned models, the TV viewing time with the total self-reported sedentary time, no statistically significant association was detected between this time and IR ( $p=0.126$ , Model 1) (Table 3). Further adjustment for MVPA (Model 2) and WC (Model 3) does not alter this association, while MVPA was inversely associated and WC positively related to HOMA-IR (Table 3). Entering a two-way interaction term between gender and total self-reported time in the Model 3, a significant modification on the association between this time and HOMA-IR by gender was detected ( $p$  for interaction between TV viewing time and gender= $0.024$ ). Thereinafter, a stratified analysis by gender was conducted indicating that the total self-reported sedentary time is positively related to IR only among girls ( $\beta$ -coefficient (95% CI):  $0.005$  ( $0.002 - 0.009$ ),  $p=0.006$ ). Similar results were found among normal weight adolescents (Tables 4a), while the total self-reported sedentary time was found to be significantly positively associated with HOMA-IR among overweight/obese even after controlling for central obesity and MVPA (Table 4b). On the other hand, MVPA was inversely related to HOMA-IR both in overweight/obese and normal weight adolescents even after controlling for the total self-reported sedentary time (Tables 4a and 4b).

	Total	By gender		By BMI status	
		Male	Female	Normal weight	Obese/Overweight
<b>Objectively measured PA</b>					
Time spent inactive (<100 counts)	-0.012	-0.064	0.004	0.011	0.095
Time spent on MVPA (>2000 counts)	-0.117*	-0.031	-0.115*	-0.111*	-0.220*
<b>Self-reported sedentary time</b>					
TV viewing	0.133*	0.094*	0.181*	0.145*	0.077
Playing computer and console games	0.061	0.109*	0.086*	0.048	0.067
Surfing by internet	-0.061	-0.108	-0.016	-0.025	-0.106
Total sedentary time	0.090*	0.064	0.149*	0.098*	0.081

\*p-value<0.05

Table 2: Spearman correlation coefficients between HOMA-IR and sedentary and physical inactivity and MVPA.

Parameters	Model 1		Model 2		Model 3	
	$\beta$ -coefficients	p-value	$\beta$ -coefficients	p-value	$\beta$ -coefficients	p-value
	(95% CI)		(95% CI)		(95% CI)	
TV viewing						
< 2h/d	Reference	-	Reference	-	Reference	-
$\geq 2$ h/d	0.120 (0.033 – 0.207)	0.007	0.160 (0.058 – 0.261)	0.002	0.130 (0.038 – 0.223)	0.005
MVPA	-	-	-0.004 (-0.006 – (-0.001))	0.001	-0.003 (-0.005 – (-0.001))	0.002
WC	-	-	-	-	0.030 (0.025 – 0.036)	<0.001
Total self-reported sedentary time (per 10 min increase)	0.002 (-0.005–0.004)	0.126	0.003 (-0.001 – 0.005)	0.06	0.002 (-0.001 – 0.005)	0.066
MVPA	-	-	-0.004 (-0.006 – (-0.001))	0.002	-0.003 (-0.005 – (-0.001))	0.002
WC	-	-	-	-	0.031 (0.025 – 0.037)	<0.001

Model 1: After controlling for age, sex, Tanner stage, total energy intake, simple carbohydrate and fat intake  
 Model 2: After controlling for age, sex, Tanner stage, total energy intake, simple carbohydrate and fat intake and MVPA  
 Model 3: After controlling for age, sex, Tanner stage, total energy intake, simple carbohydrate and fat intake, MVPA and WC  
 MVPA: Moderate-to-Vigorous Physical Activity; WC: Waist Circumference

Table 3: Results from multilevel multiple linear regressions for the association between sedentary time and log-transformed values of HOMA-IR.

Parameters	Model 1		Model 2		Model 3	
	$\beta$ -coefficients (95% CI)	p-value	$\beta$ -coefficients (95% CI)	p-value	$\beta$ -coefficients (95% CI)	p-value
TV viewing						
< 2h/d	Reference	-	Reference	-	Reference	-
$\geq$ 2h/d	0.114 (0.023 – 0.204)	0.014	0.124 (0.018 – 0.231)	0.022	0.119 (0.015 – 0.223)	0.025
MVPA	-	-	-0.003 (-0.005 – (-0.0006))	0.012	-0.002 (-0.005 – (-0.004))	0.017
WC	-	-	-	-	0.025 (0.015 – 0.035)	<0.001
Total self-reported sedentary time (per 10 min increase)	0.001 (-0.001–0.003)	0.352	0.001 (-0.001 – 0.004)	0.25	0.001 (-0.001 – 0.004)	0.388
MVPA	-	-	-0.003 (-0.005 – (-0.0004))	0.002	-0.003 (-0.005 – (-0.0003))	0.023
WC	-	-	-	-	0.025 (0.015 – 0.036)	<0.001

Model 1: After controlling for age, sex, Tanner stage, total energy intake, simple carbohydrate and fat intake

Model 2: After controlling for age, sex, Tanner stage, total energy intake, simple carbohydrate and fat intake and MVPA

Model 3: After controlling for age, sex, Tanner stage, total energy intake, simple carbohydrate and fat intake, MVPA and WC

MVPA: Moderate-to-Vigorous Physical Activity; WC: Waist Circumference

**Table 4a:** Results from multilevel multiple linear regressions for the association between sedentary time and log-transformed values of HOMA-IR, among normal weight adolescents.

Parameters	Model 1		Model 2		Model 3	
	$\beta$ -coefficients (95% CI)	p-value	$\beta$ -coefficients (95% CI)	p-value	$\beta$ -coefficients (95% CI)	p-value
TV viewing						
< 2h/d	Reference	-	Reference	-	Reference	-
$\geq$ 2h/d	0.073 (-0.135 – 0.281)	0.492	0.076 (-0.151 – 0.304)	0.509	0.117 (-0.096 – 0.332)	0.283
MVPA	-	-	-0.009 (-0.015 – (-0.003))	0.002	-0.007 (-0.013 – (-0.001))	0.012
WC	-	-	-	-	0.026 (0.013 – 0.040)	<0.001
Total self-reported sedentary time (per 10 min increase)	0.004 (-0.001–0.001)	0.114	0.003 (-0.003 – 0.009)	0.323	0.006 (0.0003 – 0.001)	0.038
MVPA	-	-	-0.009 (-0.014 – (-0.004))	0.001	-0.007 (-0.012 – (-0.002))	0.005
WC	-	-	-	-	0.027 (0.011 – 0.043)	<0.001

Model 1: After controlling for age, sex, Tanner stage, total energy intake, simple carbohydrate and fat intake

Model 2: After controlling for age, sex, Tanner stage, total energy intake, simple carbohydrate and fat intake and MVPA

Model 3: After controlling for age, sex, Tanner stage, total energy intake, simple carbohydrate and fat intake, MVPA and WC

MVPA: Moderate-to-Vigorous Physical Activity; WC: waist circumference

**Table 4b:** Results from multilevel multiple linear regressions for the association between sedentary time and log-transformed values of HOMA-IR, among overweight/obese adolescents.

## Discussion

To the best of our knowledge, this is the first study examining this association in such European population. The present findings revealed no association between objectively measured sedentary life and IR, while a significant association between self-reported sedentary and HOMA-IR was detected even after controlling for central obesity, MVPA and total energy intake. In particular, it was found that adolescents exceeding the limit of 2 h/d TV viewing had significantly higher HOMA-IR levels and this relationship was identified only among normal weight adolescents. Moreover, the association of total self-reported sedentary time (including TV viewing, playing computer and/or console games and surfing on internet) with IR among normal weight adolescents was found to be modified by gender and a positive association was detected only

among girls, while increased total self-reported sedentary time was found to be related with higher HOMA-IR levels in both overweight/obese boys and girls.

Although this is one of the few study that detect an association between TV viewing and IR among youths, these findings corroborate previous findings in adult populations that indicate that sedentary lifestyle, characterized by time spent watching TV, was significantly associated with an increased risk for abnormal glucose metabolism and metabolic syndrome, independent of the effect of physical activity [22-25,39]. As concerns the association between objectively measured sedentary time and IR, our results are in disagreement with those reported for 9 to 10-yr-old Portuguese children [13] and adults [20], while are in the same line with those detected in adults with a family history of type 2 diabetes [21]. Differences between studies are likely

explained by discrepancies in study design (i.e. cross-sectional or prospective studies), in population characteristics (i.e., age, diabetes risk and obesity status) and maybe in methodology used for assessing and defining sedentary time (i.e. thresholds etc). Future studies are needed to determine whether objectively measured sedentary time predicts IR among adolescents.

The positive association observed between TV viewing time and IR risk could be explained by a number of mechanisms. Firstly, it has been found that TV viewing is highly associated with poor eating habits and particularly snacking behaviour while watching TV [40]. Although, no detailed data about TV viewing and eating habits has been considered in the present study, we did have information about the daily averaged dietary intake. Even after including total energy intake, fat and simple carbohydrate intake as potential confounders, we still found a significant positive association between TV viewing and IR. Therefore, this association cannot be attributed fully in the effect of poor eating habits while watching TV. Secondly, due to modest inverse correlation between PA and physical inactivity (or sedentary behaviour), the effect of the length time spent watching TV on the IR could possibly be confounded by PA. However, in our study, even after adjusting for MVPA, we still found HOMA-IR levels to be significantly related to the time spent viewing TV.

Despite the large sample size and the diversity of study population that strengthen the generalization of our findings, several limitations need consideration when interpreting the results. Firstly, HELENA study was cross-sectional, thus limiting inferences for causal associations between sedentary behaviours and IR. Secondly, the gold standard for measuring IR is the FSIVGIT. However, it is difficult to implement in population studies. Therefore, an indirect method for IR identification (HOMA-IR) was used. Thirdly, although adjustment for the confounding effect of gender sexual maturity, birth weight and total or central fat mass and dietary factors was conducted, it is possible that other unmeasured confounders such as genetic variation could explain the current findings. Fourthly, the use of accelerometers as a valid method to objectively measure PA subcomponents, involve some limitations. In particular, accelerometers cannot record water activities, such as swimming and water sports, because they are not waterproof. Furthermore, the uniaxial accelerometers are limited in capturing a wide range of stationary activities such as bicycling, weight lifting and generally body movements which include limited movement of the upper body, thus lacking in precision of acquired information on sedentary levels. Finally, the findings of the current study may be limited by the use of the specific thresholds to summarize accelerometer. However, the threshold of 100 cpm to define sedentary behaviour has been previously proposed by Treuth et al. [41-44].

## Conclusion

In conclusion, the results of the present study indicate that time spent watching TV and at MVPA is related to IR independent of central fat mass and total energy intake in normal weight European adolescents, while MVPA seems to protect adolescents from developing IR even among overweight/obese adolescents. Therefore, public health makers should focus on designing and implementing intervention programmes aiming at reducing sedentary behaviours by setting upper levels of sedentarily and increasing overall involvement of European adolescents in different types of moderate-intensity activities. Such interventions could contribute into primary prevention of metabolic disorders at young age.

## References

1. Viner RM, Segal TY, Lichtarowicz-Krynska E, Hindmarsh P (2005) Prevalence of the insulin resistance syndrome in obesity. *Arch Dis Child* 90:10-14.
2. Manios Y, Moschonis G, Kurlaba G, Bouloubasi Z, Grammatikaki E, et al. (2008) Prevalence and independent predictors of insulin resistance in children from Crete, Greece: The Children Study. *Diabet Med* 25:65-72.
3. Caceres M, Teran CG, Rodriguez S, Medina M (2008) Prevalence of insulin resistance and its association with metabolic syndrome criteria among Bolivian children and adolescents with obesity. *BMC Pediatr* 8:31.
4. Lee JM, Okumura MJ, Davis MM, Herman WH, Gurney JG (2006) Prevalence and determinants of insulin resistance among U.S. adolescents: A population-based study. *Diabetes Care* 29:2427-2432.
5. Valerio G, Licenziati MR, Iannuzzi A, Franzese A, Siani P, et al (2006) Insulin resistance and impaired glucose tolerance in obese children and adolescents from Southern Italy. *Nutr Metab Cardiovasc Dis* 16:279-284.
6. Chiarelli F, Marcovecchio ML (2008) Insulin resistance and obesity in childhood. *Eur J Endocrinol* 1:S67-74.
7. Lee JM (2006) Insulin resistance in children and adolescents. *Rev Endocr Metab Disord* 7:141-147.
8. Barness LA, Opitz JM, Gilbert-Barness E (2007) Obesity: genetic, molecular, and environmental aspects. *Am J Med Genet A* 143:3016-3034.
9. Korner A, Kiess W, Stumvoll M, Kovacs P (2008) Polygenic contribution to obesity: Genome-wide strategies reveal new targets. *Front Horm Res* 36:12-36.
10. Kahn HS, Imperatore G, Cheng YJ (2005) A population-based comparison of BMI percentiles and waist-to-height ratio for identifying cardiovascular risk in youth. *J Pediatr* 146:482-488.
11. Mrdjenovic G, Levitsky DA (2003) Nutritional and energetic consequences of sweetened drink consumption in 6- to 13-year-old children. *J Pediatr* 142:604-610.
12. Gutin B, Johnson MH, Humphries MC, Hatfield-Laube JL, Kapuku GK, et al. (2007) Relationship of visceral adiposity to cardiovascular disease risk factors in black and white teens. *Obesity (Silver Spring)* 15:1029-35.
13. Brage S, Wedderkopp N, Ekelund U, Franks PW, Wareham NJ (2004) Objectively measured physical activity correlates with indices of insulin resistance in Danish children. The European Youth Heart Study (EYHS). *Int J Obes Relat Metab Disord* 28:1503-1508.
14. Rizzo NS, Ruiz JR, Oja L, Veidebaum T, Sjostrom M (2008) Associations between physical activity, body fat, and insulin resistance (homeostasis model assessment) in adolescents: The European Youth Heart Study. *Am J Clin Nutr* 87:586-592.
15. Imperatore G, Cheng YJ, Williams DE, Fulton J, Gregg EW (2006) Physical activity, cardiovascular fitness, and insulin sensitivity among U.S. adolescents: the National Health and Nutrition Examination Survey, 1999-2002. *Diabetes Care* 29:1567-72.
16. Bunt JC, Salbe AD, Harper IT, Hanson RL, Tataranni PA (2003) Weight, adiposity, and physical activity as determinants of an insulin sensitivity index in pima Indian children. *Diabetes Care* 26:2524-2530.
17. Schmitz KH, Jacobs DR, Hong CP, Steinberger J, Moran A, et al. (2002) Association of physical activity with insulin sensitivity in children. *Int J Obes Relat Metab Disord* 26:1310-1316.
18. Ku CY, Gower BA, Hunter GR, Goran MI (2000) Racial differences in insulin secretion and sensitivity in prepubertal children: Role of physical fitness and physical activity. *Obes Res* 8:506-515.
19. Helmerhorst HJ, Wijndaele K, Brage S, Wareham NJ, Ekelund U (2009) Objectively measured sedentary time may predict insulin resistance independent of moderate- and vigorous-intensity physical activity. *Diabetes* 58:1776-1779.
20. Ekelund U, Brage S, Griffin SJ, Wareham NJ (2009) Objectively measured moderate- and vigorous-intensity physical activity but not sedentary time predicts insulin resistance in high-risk individuals. *Diabetes Care* 32:1081-1086.
21. Sardinha LB, Andersen LB, Anderssen SA, Quiterio AL, Ornelas R, et al. (2008) Objectively measured time spent sedentary is associated with insulin resistance independent of overall and central body fat in 9- to 10-year-old Portuguese children. *Diabetes Care* 31:569-575.

22. Dunstan DW, Salmon J, Healy GN, Shaw JE, Jolley D, et al. (2007) Association of television viewing with fasting and 2-h postchallenge plasma glucose levels in adults without diagnosed diabetes. *Diabetes Care* 30:516-522.
23. Dunstan DW, Salmon J, Owen N, Armstrong T, Zimmet PZ, et al. (2004) Physical activity and television viewing in relation to risk of undiagnosed abnormal glucose metabolism in adults. *Diabetes Care* 27:2603-2609.
24. Dunstan DW, Salmon J, Owen N, Armstrong T, Zimmet PZ, et al. (2005) Associations of TV viewing and physical activity with the metabolic syndrome in Australian adults. *Diabetologia* 48:2254-2261.
25. Hu FB, Li TY, Colditz GA, Willett WC, Manson JE (2003) Television watching and other sedentary behaviors in relation to risk of obesity and type 2 diabetes mellitus in women. *JAMA* 289:1785-1791.
26. Ruiz JR, Ortega FB, Martínez-Gómez D, Labayen I, Moreno LA, et al. (2011) Objectively measured physical activity and sedentary time in European adolescents: the HELENA study. *Am J Epidemiol* 174:173-184.
27. Rey-López JP, Vicente-Rodríguez G, Ortega FB, Ruiz JR, Martínez-Gómez D, et al. (2010) Sedentary patterns and media availability in European adolescents: The HELENA study. *Prev Med* 51:50-55.
28. Moreno LA, De Henauw S, González-Gross M, Kersting M, Molnár D, et al. (2008) Design and implementation of the Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study. *Int J Obes (Lond)* 32 Suppl 5:S4-11.
29. Béghin L, Castera M, Manios Y, Gilbert CC, Kersting M, et al. (2008) Quality assurance of ethical issues and regulatory aspects relating to good clinical practices in the HELENA Cross-Sectional Study. *Int J Obes (Lond)* 32 Suppl 5:S12-18.
30. Nagy E, Vicente-Rodríguez G, Manios Y, Béghin L, Iliescu C (2008) Harmonization process and reliability assessment of anthropometric measurements in a multicenter study in adolescents. *Int J Obes (Lond)*, 2008. 32 Suppl 5:S58-65.
31. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH (2000) Establishing a standard definition for child overweight and obesity worldwide: international survey. *Bmj* 320:1240-1243.
32. Lohman TG, Roche AF, Martorell R (1988) *Anthropometric Standardization Reference Manual*. Human Kinetics Books: Champaign, Illinois.
33. Tanner JM, Whitehouse RH (1976) Clinical longitudinal standards for height, weight, height velocity, weight velocity, and stages of puberty. *Arch Dis Child* 51:170-179.
34. Hagströmer M1, Bergman P, De Bourdeaudhuij I, Ortega FB, Ruiz JR, et al. (2008) Concurrent validity of a modified version of the International Physical Activity Questionnaire (IPAQ-A) in European adolescents: The HELENA Study. *Int J Obes (Lond)* 32 Suppl 5:S42-8.
35. Vicente-Rodríguez G, Rey-López JP, Martín-Matillas M, Moreno LA, Wärnberg J, et al (2008) Television watching, videogames, and excess of body fat in Spanish adolescents: the AVENA study. *Nutrition* 24:654-662.
36. <http://pediatrics.aappublications.org/content/107/2/423.long>
37. Biró G, Hulshof KF, Ovesen L, Amorim Cruz JA; EFCOSUM Group (2002) Selection of methodology to assess food intake. *Eur J Clin Nutr* 56:S25-S32.
38. Vereecken CA, Covents M, Matthys C, Maes L (2005) Young adolescents' nutrition assessment on computer (YANA-C). *Eur J Clin Nutr* 59:658-667.
39. Kersting M, Sichert-Hellert W, Vereecken CA, Diehl J, Béghin L, et al. (2008) Food and nutrient intake, nutritional knowledge and diet-related attitudes in European adolescents. *Int J Obes (Lond)* 32 Suppl 5:S35-41.
40. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, et al. (1985) Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 28:412-419.
41. Gonzalez-Gross M, Breidenassel C, Gomez-Martinez S, Ferrari MBL, Spinneker A, et al. (2008) Sampling and processing of fresh blood samples within a European multicenter nutritional study: evaluation of biomarker stability during transport and storage. *Int J Obes (Lond)* 32:S66-75.
42. Chang PC, Li TC, Wu MT, Liu CS, Li CI, et al (2008) Association between television viewing and the risk of metabolic syndrome in a community-based population. *BMC Public Health* 8:193.
43. Jeffery RW, French SA (1998) Epidemic obesity in the United States: are fast foods and television viewing contributing? *Am J Public Health* 88:277-280.
44. Treuth MS, Schmitz K, Catellier DJ, McMurray RG, Murray DM, et al. (2004) Defining accelerometer thresholds for activity intensities in adolescent girls. *Med Sci Sports Exerc* 36:1259-1266.