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

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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. Homeostatic 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 (µIU/mL) × GF (mmol/l)/22.5 (to convert IF values in µIU/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 ≥ 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 (r=−0.117, p=0.023). Multilevel linear regression analysis revealed that adolescents watching TV ≥ 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...
(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 as 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 sedentary 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 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 Frankfort 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 (m²) [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 (≥ 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 was 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 (µU/mL) × GF (mmol/l))/22.5 (to convert IF values in µU/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 ± 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 analyzed through linear regression model.
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 β-coefficients and 95% confidence interval (95% CI). P-values<0.05 between PA subcomponent and HOMA-IR. The results are presented from two-sided hypotheses are considered as statistically significant.

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

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<table>
<thead>
<tr>
<th>Parameters</th>
<th>Total (N=1089)</th>
<th>Males (N=580)</th>
<th>Females (N=509)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>14.83 ± 1.2</td>
<td>14.76±1.2</td>
<td>14.70 ±1.1</td>
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<td>Anthropometric measures</td>
<td></td>
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<td></td>
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<tr>
<td>BMI (kg/m²)</td>
<td>21.4 ± 3.7</td>
<td>21.4 ± 4.0</td>
<td>21.3 ± 3.3</td>
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<tr>
<td>Waist circumference (cm)</td>
<td>72.4 ± 8.6</td>
<td>74.4 ± 9</td>
<td>70.7 ± 7.8</td>
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<td>Tanner stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.70%</td>
<td>1.60%</td>
<td>0.6%</td>
</tr>
<tr>
<td>2</td>
<td>6.20%</td>
<td>8.10%</td>
<td>5.50%</td>
</tr>
<tr>
<td>3</td>
<td>20.90%</td>
<td>20.10%</td>
<td>18.50%</td>
</tr>
<tr>
<td>4</td>
<td>42.90%</td>
<td>41.60%</td>
<td>38.10%</td>
</tr>
<tr>
<td>5</td>
<td>29.30%</td>
<td>28.60%</td>
<td>26.10%</td>
</tr>
<tr>
<td>Self-reported sedentary time (min/day)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TV viewing</td>
<td>107 (58, 167)</td>
<td>107 (70, 167)</td>
<td>107 (58, 167)</td>
</tr>
<tr>
<td>Playing on computer and console games</td>
<td>56 (9, 124)</td>
<td>105 (39, 183)</td>
<td>24 (0, 75)</td>
</tr>
<tr>
<td>Surfing by Internet</td>
<td>45 (11, 91)</td>
<td>45 (11, 90)</td>
<td>45 (11, 107)</td>
</tr>
<tr>
<td>Total sedentary time (min/day)</td>
<td>227 (141, 349)</td>
<td>272 (180, 399)</td>
<td>193 (120, 298)</td>
</tr>
<tr>
<td>Objectively measured PA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time spent inactive (&lt;100counts/min)</td>
<td>543 ± 86</td>
<td>535.96 ± 93</td>
<td>547.79 ± 78</td>
</tr>
<tr>
<td>Time spent on MVPA (&gt;2000counts/min)</td>
<td>59 ± 24</td>
<td>69.24 ± 25.11</td>
<td>51.07 ± 20.30</td>
</tr>
<tr>
<td>Biochemical measurements</td>
<td></td>
<td></td>
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<tr>
<td>Insulin (μIU/mL)</td>
<td>8.65 (6.20, 12.0)</td>
<td>8.17 (5.93, 11.50)</td>
<td>9.12 (6.57, 12.30)</td>
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<tr>
<td>HOMA-IR</td>
<td>1.95 (1.37, 2.72)</td>
<td>1.87 (1.33, 2.69)</td>
<td>2.04 (1.39, 2.77)</td>
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<tr>
<td>Energy and macronutrients intake</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total energy (kcal/day)</td>
<td>2261 ± 1018</td>
<td>2646 ± 1134</td>
<td>1928 ± 763</td>
</tr>
<tr>
<td>Total carbohydrate (gr./day)</td>
<td>273 ± 129</td>
<td>318 ± 149</td>
<td>233 ± 91</td>
</tr>
<tr>
<td>Total fat (gr./day)</td>
<td>91 ± 50</td>
<td>106 ± 56</td>
<td>77 ± 40</td>
</tr>
</tbody>
</table>

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 ≥ 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 ≥ 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).

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 significantly 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 (β-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).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β-coefficients (95% CI)</td>
<td>p-value</td>
<td>β-coefficients (95% CI)</td>
</tr>
<tr>
<td>TV viewing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 2 h/d</td>
<td>Reference</td>
<td>-</td>
<td>Reference</td>
</tr>
<tr>
<td>≥ 2 h/d</td>
<td>0.120 (0.033 – 0.207)</td>
<td>0.007</td>
<td>0.160 (0.058 – 0.261)</td>
</tr>
<tr>
<td>MVPA</td>
<td>-</td>
<td>-</td>
<td>-0.004 (-0.006 – (-0.001))</td>
</tr>
<tr>
<td>WC</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total self-reported sedentary time (per 10 min increase)</td>
<td>0.002 (-0.005–0.004)</td>
<td>0.126</td>
<td>0.003 (-0.001 – 0.005)</td>
</tr>
<tr>
<td>MVPA</td>
<td>-</td>
<td>-</td>
<td>-0.004 (-0.006 – (-0.001))</td>
</tr>
<tr>
<td>WC</td>
<td>-</td>
<td>-</td>
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</tbody>
</table>

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


36. http://pediatrics.aappublications.org/content/107/2/423.long


